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Antenatal predictors of early mother-to- infant bonding failure A prospective cohort study

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University of London

Antenatal predictors of early mother-to-infant bonding failure: A prospective cohort study

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**A thesis submitted in fulfilment of the requirements for the
degree of Doctor of Philosophy**

Florence Nightingale Faculty of Nursing & Midwifery

King's College London

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Abstract

Background

The majority of women who have given birth will develop affection for their infants, however some have prolonged problems developing a loving attitude, leading to impaired mother-infant bonding. Some studies have found an association between postnatal depression and poor mother-infant bonding. On the other hand, little is known about the antenatal predictors of this problem.

Aim

The aim of this study was to determine if it is possible to predict during pregnancy which women will develop impaired mother-infant bonding; and to assess whether having a high risk pregnancy could affect this bond.

Method

A prospective cohort study was conducted with women who were recruited from one London Hospital between 2008 and 2012. Psychometric data were collected from 300 women in late pregnancy; 223 were followed up at six weeks postnatal using self-administered questionnaires. Sixty-six of these women had a high risk pregnancy. Saliva samples were collected from a subsample of participants (N=46) as part of a pilot study to physiologically measure cortisol and alpha-amylase (as biological markers of maternal stress and depression) embedded within the main study.

Results

There was a lower risk of impaired mother-infant bonding at six weeks postnatal, if the woman had good fetal bonding in late pregnancy (OR=0.89, 95%CI=0.83-0.94, $p<0.001$), but a higher risk of impaired maternal bonding at this time, if the woman had symptoms of depression during pregnancy (OR=1.12, 95%CI=1.11-1.41, $p<0.05$). Another determinant of poor mother-infant bonding in the study was postnatal depressive symptoms and having an epidural analgesia during labour and birth, although reasons for this need further consideration. There were no significant differences in mother to infant bonding status between women who had a high or a low risk pregnancy.

Conclusion

Maternal mental health and fetal bonding emerged as the strongest predictors of impaired maternal-infant bonding, together with the negative association with having an epidural analgesia. The findings from this study highlight the importance of training for clinicians to be aware that mother-infant bonding problem can develop during pregnancy. The negative effect of epidural analgesia on mother-infant bonding warrants further investigation.

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Dedication

“To God be the Glory”

I dedicate this PhD thesis to:

- My husband Fidelis Osuji, he has always believed in me. I could not have accomplished as much as I have without his love, support, understanding and patience.
- To my children: Ezinne, Tochi, Chimaobi and Ugonna Osuji. May they understand the journey of knowledge, courage and be able to reach their full potential.
- In memory of my late little brother, Chima Agbagwara who died at the age of 24. His memory inspired me to make this dream a reality. Your wisdom and humours are with me. You will always be in my thoughts.

CHAPTER 1 INTRODUCTION

Mother-infant bonding has attracted the attention of researchers for several decades (Klaus and Kennell, 1976, Kopelman et al., 1978, Svejda et al., 1980, Crouch and Manderson, 1995). While the initial focus of mother-infant bonding as described by Klaus and Kennell in 1970's was to promote early physical contact between the mother and her infant, it is now widely believed that physical contact immediately after birth is desirable but it is not necessary for the development of mother-infant bonding (Chess and Thomas, 1983, Eyer, 1994, Kennell and Klaus, 1998, Bicking Kinsey and Hupcey, 2013). In recent years, research in this area has focused mainly on factors that facilitate or restrain mother-infant bonding during the postnatal period; however, there are some discrepancies in these findings. There are also inconsistencies in the definition and instruments used to assess mother-infant bonding.

Most women develop affection towards their infants in the early hours and weeks postnatal, on the other hand, some may not develop this affection towards their infants and may be indifferent or disappointed with their infants in early weeks postnatal (Kumar, 1997, Brockington, 2006). Research in this area is important because failure of mothers to establish a strong bond with their child during infancy may have a negative effect on the mother-infant interaction leading to poor mother-to-infant relationship (Klaus et al., 1996, Brockington, 2008).

The subject of this PhD thesis is impaired mother-infant bonding. Few empirical studies have examined if there are antenatal determinants of mother-infant bonding problems. Screening for poor mother-infant bonding is not currently part of routine postnatal care, yet mother-infant bonding is considered as one aspect of the infant developmental process, which if successfully achieved, can lead to a strong healthy relationship between the mother and her infant and promote positive self-concept for the child later in life (Madrid et al., 2006, Kinsey et al., 2014).

Maternal 'bonding' is often confused with 'attachment'. Mother-infant bonding refers to the affectionate feelings of a woman towards her infant, and is viewed as an important part of postpartum development (Brockington, 1996). Maternal bonding differs from attachment, with attachment defined as "a strong emotional tie from the infant to his/her caregiver that develops over time, and results in a desire to maintain proximity" (Bowlby, 1958). For some researchers, maternal bonding after birth is thought to be an adaptive mechanism that is biologically driven mainly by the hormone oxytocin (Feldman et al., 2007, Galbally et al., 2011), a mammalian neurohypophysial hormone strongly associated with social and affiliative behaviour (Insel, 2010).

In this study, the term 'mother-to-infant bonding' was used to refer to a woman's feelings towards her infant, expressed by her affectionate and protective behaviour. This study focused primarily on maternal feeling as an indicator of an early mother-infant relationship (as a one way process), rather than as a two-way process, seen in the later mother-infant relationship, which includes

mother-infant synchrony (Reyna and Pickler, 2009, Feldman, 2012), mother-infant interaction (Murray et al., 1996, Stanley et al., 2004, Logsdon et al., 2006) and mother-infant dyadic regulation (Barlow, 2012), which require some form of mutual responsiveness, with an observable pattern that is mutually regulated and reciprocal (Reyna and Pickler, 2009).

This thesis presents findings of two studies, the main study and an embedded pilot study undertaken alongside the main study as an opportunity to use a subset of women in the study cohort to assess whether using biological measures of stress (i.e., salivary alpha-amylase and cortisol) during pregnancy could be used to identify women who may go on to develop postnatal early mother-infant bonding problems.

1.1 Background of the study

The adverse effect of maternal bonding difficulties on the quality of mother-to-infant interactions and relationship with the infant has been documented (Kumar, 1997, Brockington, 2004). Although the quality of paternal bonding (Feldman, 2012, Hall et al., 2014) may also contribute to infant development, the maternal relationship is the focus of this study. A mother's positive emotions and attitudes towards her infant are essential for well-being and development of the infant, because the mother, who is usually the primary care giver, is the most important source of stimulation for the infant (Cirulli et al., 2003, Logsdon et al., 2006). These positive emotions and attitudes facilitate later mother-infant interactions and relationship with the infant (Kumar, 1997, Madrid et al., 2006).

The development of maternal feelings of love or an emotional tie to the infant has been shown to originate during pregnancy (Condon, 1993, Siddiqui and Hägglöf, 2000, Shieh et al., 2001). In some women, it may start as early as the first trimester of pregnancy and increase as the pregnancy progresses (Fleming et al., 1997, Laxton-Kane and Slade, 2002, Righetti et al., 2005), while some women may not develop feelings of maternal affection until after the baby is born, which may underpin the development of a woman's relationship with her infant (Kumar, 1997, O'Higgins et al., 2013).

It has been proposed that mother's affective mood is an important factor for a healthy mother-infant interaction (Righetti-Veltema et al., 2002). That is, mother-infant bonding is viewed as the foundation for the infant's later attachment, which forms the basis for his or her sense of self (Klaus and Kennell, 1982, Madrid et al., 2006). Although most women successfully develop a healthy relationship with their infant, some women, for example those with depression during the postnatal period, have difficulties with this bonding process (Kumar, 1997).

One of the leading researchers in this field is Professor Ian Brockington, a UK based psychiatrist. In a seminal 1996 publication on mother-infant bonding disorders, Brockington referred to this "as a mother-to-infant relationship disorder" or simply a "bonding disorder". He described the symptoms of this disorder as a mother's ambivalence, or the loss of the maternal emotional

response to her infant through the demonstration of behaviour such as aversion. In extreme cases, it can lead to rejection of the infant, hatred, anger and/or child abuse (Brockington, 1996).

In a later publication, Brockington (2004) also suggested that this disorder was a specific phenomenon on its own and not simply a feature of maternal depression because it had been identified in both depressed and non-depressed mothers. Brockington and colleagues proposed that if this disorder was identified, and was not considered or labelled as a problem only associated with postnatal depression, interventions to improve maternal bonding could be implemented. Therefore the early detection of this maternal bonding problem, preferably during the antenatal period, was viewed as crucial due to the potential long-term negative effect on the mother-infant relationship.

1.1.1 Maternal emotional health during pregnancy

It is widely recognised that pregnancy is a period of increased vulnerability to mental disorders, such as depression and anxiety (Campagne, 2004, Lancaster et al., 2010, Nasreen et al., 2011, Glover, 2014). An adverse effect of antenatal anxiety on mother-infant bonding was reported by (Figueiredo and Costa, 2009), a plausible association since maternal antenatal stress and anxiety have been found to predict postnatal depression (Banti et al., 2011) which in turn is a risk factor associated with impaired mother-infant bonding. Additionally as maternal bonding fundamentally begins during pregnancy (Muller, 1996, Siddiqui and Hägglöf, 2000, Dubber et al., 2014), antenatal depression or anxiety could affect the early bonding process, impairing the mother-infant relationship after birth.

In addition to the common stressors that most people have to deal with, (e.g. divorce, death of a loved one, or day to day concerns, such as domestic affairs, financial or relationship problems), pregnant women face other potential stress factors, including pregnancy-specific anxiety (e.g. fear of infant survival and the woman's own health) (Mulder et al., 2002, Schetter and Tanner, 2012, Henderson and Redshaw, 2013). One group of women found to have potentially higher rates of anxiety during pregnancy are women with high obstetric risk factors (Kemp and Hatmaker, 1989, McCain and Deatruck, 1994, Kurki et al., 2000, King et al., 2010). A pregnancy is labelled 'high risk' when there is evidence that a threat exists to the health of the mother and/or the fetus (Kemp and Hatmaker, 1989).

A descriptive cross-sectional study from the USA compared the risk of depressive symptoms in 129 women with either high or low obstetric risk factors, using the Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987) and a structured semi-structured diagnostic interviews developed by (Summerfeldt and Antony, 2002). They found a higher prevalence rate of major depressive disorder in women with high obstetric risk factors than among the low risk group (Brandon et al., 2008).

Similarly, King et al. (2010) conducted a study in the UK to compare the emotional state of 60 antenatal women with high obstetric risk factors in pregnancy and 60 controls (antenatal women with no obstetric risk factors), using the EPDS and Spielberger State-Trait Anxiety Inventory (Spielberger, 1983) at around 32 weeks gestation. They found that women with high obstetric

risk factors, such as hyperemesis gravidarum, pre-eclampsia and obstetric cholestasis, had more anxiety and depression symptoms compared to the controls. Despite these studies, there is limited knowledge of the effect of high risk pregnancy on maternal affectionate feelings towards their infants. It is therefore important to investigate if increased stress and anxiety found in women with high obstetric risk factors during pregnancy could adversely affect the mother-to-infant bond as this could inform the development of more effective support for women who have a high risk pregnancy.

1.1.2 Bonding verses attachment

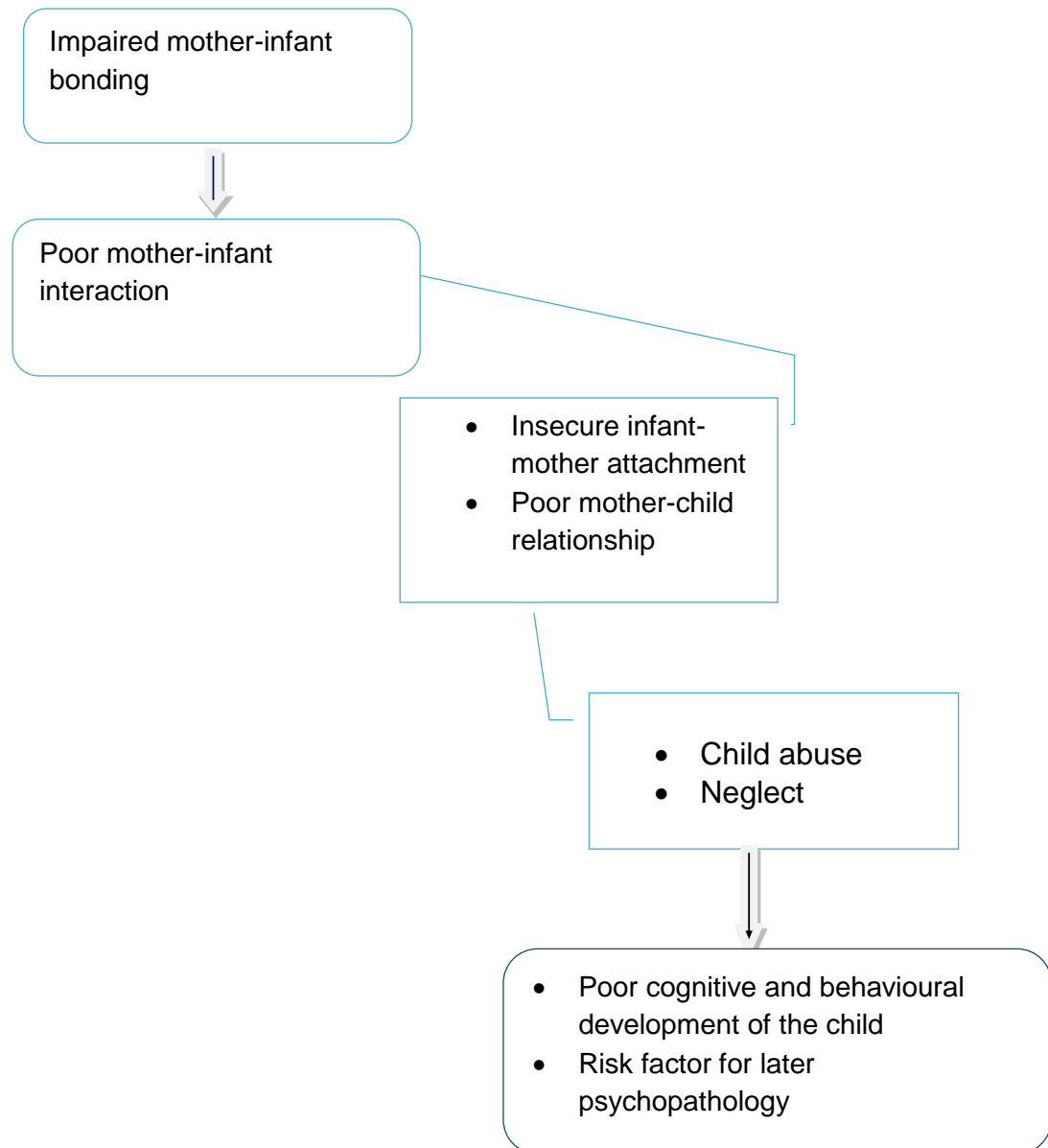
As referred to earlier, mother-infant bonding and mother-infant attachment are sometimes used interchangeably and incorrectly in the literature (Brockington, 2011). A recent review of the current state of the science of maternal–infant bonding found that some authors still use the term maternal-infant bonding and maternal-infant attachment interchangeably, creating inconsistencies in the linguistic use of the term (Bicking Kinsey and Hupcey, 2013).

According to Symanski (1992); Benoit (2004); Redshaw and Martin (2013), attachment is not ‘bonding’. By way of explanation, the term mother-infant bonding refers to the emotional affection that the mother feels towards her infant; the process that occurs from the first moment that a mother begins to feel connected to her infant (Erickson, 1996, Eksirinit, 2012). These feelings may begin in-utero, immediately after birth or may develop later (Taylor et al., 2005, Van den Bergh and Simons, 2009, Yoshida et al., 2012). Attachment, on the other hand, is the outcome of the bonding process (Erickson, 1996) and is described from the perspective of the infant (Symanski, 1992). Attachment

relies on the baby being able to show responses to the mother, when the baby is able to focus on its mother's face and smile, which is when attachment becomes a two-way interaction (Taylor et al., 2005).

As the quality of mother-to-infant interaction is associated with the quality of infant-to-mother attachment (Braungart-Rieker, 2001), maternal negative emotions towards the infant may affect the quality of maternal interaction and sensitivity, which may in turn negatively affect the quality of infant-to-mother attachment. Consequences of poor-mother infant interactions include poor social and cognitive outcomes (Murray et al., 1996), insecure attachment (Coyl et al., 2002, Miller et al., 2002), later anxiety and depression (Schmid et al., 2011) which could also affect the child's cognitive and behavioural development (Easterbrooks et al., 2012, Milgrom and Holt, 2014). A summary of potential outcomes of impaired mother-infant bonding identified from literature is presented in Figure1.1.

Figure 1-1 Potential outcomes of impaired -mother-infant bonding



1.2 Significance of the study

The quality of the relationship between infants and parents is recognised as an important factor influencing a child's development (Pisoni et al., 2014). The extent to which poor mother-infant bonding contributes to this risk however has not been established although it has been postulated (Muzik et al., 2013) that impaired mother-infant bonding may be a crucial early pathway by which a

history of maternal abuse/ and neglect from a woman's own mother which the woman may now repeat can lead to disturbed parenting practice, which may lay the foundation for adverse child outcomes (Muzik et al., 2013). Furthermore, a poor mother-infant bonding could also be a pathway to future abuse and neglect to the infant (Brockington, 2008).

The current study is important because it has been suggested that the formation of a strong bond between a mother and her infant results in more positive parenting behaviour (Klaus et al., 1996, Bicking Kinsey and Hupcey, 2013), which is associated with an improved cognitive and neurobehavioral development in a child (Choe et al., 2013, Giallo et al., 2014). Impaired maternal bonding has been associated with deficits in such positive parenting behaviour, including low sensitivity, lack of warmth, engagement and/or an inflexible attitude towards the child (Muzik et al., 2013).

It is possible that if problems in the mother-to-infant bonding can be predicted early, interventions could be implemented to identify, reduce or prevent the negative effects on the child. Moreover, as little is known about the prevalence of mother-to-infant bonding difficulties in non-clinical perinatal population, or how these develop over time (Wittkowski et al., 2007), prospective longitudinal research is needed to understand more about how bonding problems develop: when they start, precipitating factors, and how to identify indicators of poor bonding within routine antenatal care.

1.3 Research aims and objectives

The specific aims of the research presented in this thesis were as follows:

1. *To identify factors in pregnancy that could predict early mother-infant bonding problems at six weeks postnatal, focusing primarily on the maternal emotional state during pregnancy, using self-report questionnaires.*
2. *To assess if a high risk pregnancy could affect mother-to-infant bonding.*

Specific objectives were:

- *To assess whether maternal self-reported measures of anxiety, depression and other psychosocial measures in late pregnancy would predict poor mother-infant bonding at 6 weeks post birth.*
- *To examine the relationship between maternal postnatal psychometric measures and mother-infant bonding scale at 6 weeks postnatal.*
- *To assess whether having a high risk pregnancy would affect mother-infant bonding postnatal.*

1.4 Research design and method

This study used a prospective cohort design to explore data relating to impaired mother-infant bonding in a non-clinical perinatal population in one London hospital. It describes the prevalence of this disorder and interrelationships of antenatal, intrapartum and neonatal variables associated with impaired mother to infant bonding in a cohort of 223 women. Data were collected from self-complete postal questionnaires administered at two time-points:

1. *Time-point one: Self complete questionnaire between 36 weeks gestation, to determine antenatal factors associated with impaired mother-infant bonding.*
2. *Time-point two:*
 - *Data on labour, birth and neonatal outcomes collected from maternal electronic clinical records at six weeks postnatal to determine factors related to childbirth experience on mother-infant bonding.*
 - *Self-complete questionnaire collected six weeks postnatal, to determine postnatal factors associated with impaired mother-infant bonding.*

1.5 Structure of the thesis

The thesis is presented in six chapters. This introductory chapter presents a brief background and rationale for the study and outlines the research aims and objectives. Chapter two critically evaluates the literature on impaired mother-infant bonding with a specific focus on the prevalence of impaired mother-infant bonding in a non-clinical perinatal population and factors associated with mother-infant bonding problems. Chapter three provides a detailed description of the research methods used to conduct the study, data capture methods, outcome measures and approaches to data analysis. Chapter four presents the development of the pilot study, describing the aim, objectives and methods. Chapter five presents the results of the main study and the pilot study. Chapter six discusses the study findings, within the context of existing literature, study limitations, recommendations for practice, policy and future research and the study conclusion.

1.6 Chapter summary

This introductory chapter has described the rationale for, and scope of the research project presented, including the research aims and objectives, background to the study, significance of the study, theoretical foundations, and key concepts. The next chapter will critically review the relevant empirical literature on issues related to poor mother-infant bonding.

CHAPTER 2 LITERATURE REVIEW

This chapter presents an overview of the empirical literature relating to mother-infant bonding. The review relates to the concept of bonding theory, definitions of bonding and factors that could promote mother - infant bonding. In addition, the extant research on mother-infant bonding disorder is reviewed, followed by discussion of factors which may lead to impaired mother-infant bonding. The second half of this chapter also presents a comprehensive review of the literature which systematically assessed the evidence regarding factors associated with impaired mother-infant bonding in a non-clinical perinatal population. A structured review was considered necessary as it would help to identify current knowledge and issues, to inform the foundation for this study. This is important because understanding the literature is the basis for producing new evidence (Polit and Beck, 2013). The review also considered the measurement of mother-infant bonding disorder as it had implications for the selection of the instruments to measure the phenomenon in the subsequent study. The chapter is presented as follows:

- *An overview of the concept of mother-infant bonding*
- *Definition of mother-infant bonding*
- *Promotion of mother-infant bonding*
- *Mother-infant bonding disorder*
- *Factors associated with impaired mother-infant bonding*
- *A structured review of the rates and psychosocial factors associated with impaired mother-infant bonding in women with no known diagnosis of mental health problems during the perinatal period.*

2.1 Concept of mother-infant bonding

The concept of mother to infant bonding was popularised after the publication of mother to infant bonding theory first proposed by (Klaus and Kennell, 1976). The original focus of bonding theory was to promote early physical contact between a mother and her new-born. This was based on the hypothesis that there is a “sensitive” or “critical” period immediately following birth, during which mother-to infant bonding seems to occur much more readily than if a mother and her infant are separated. This concept was based on a longitudinal study which compared the behaviour of 28 low-income mothers in one American hospital. Two groups of 14 lower-class women primarily of African-American origin, who gave birth to full-term healthy infants, were compared.

The women were matched for age, social class, marital status, race and infant birth weight. They were randomly assigned into the two groups, with those in the intervention group encouraged to have additional contact with their babies in the first three days after birth, while the control group received only usual routine contact with their babies. A month after birth, the women returned to hospital for interviews and observation was made of how they interacted with their infants, which included being video-taped as they fed their babies. The intervention group women showed more soothing behaviour with their babies. They fondled them more and had more eye to eye contact when feeding them than the women in the control group. In a follow-up study one year later, in which half of the women in the original group participated, a similar positive effect was reported among the intervention group (Klaus and Kennell, 1976).

The researchers noted that the early postpartum period, especially the first hour and up to three days after birth, was a sensitive and important period for the establishment of bonding, triggered by the mother's intense affection (Klaus and Kennell 1976). The findings of this study influenced changes in routine hospital practices in the United States and elsewhere. The practice of 'rooming in', where mother and baby are not separated following transfer to the postnatal ward, gradually became part of routine post birth care in hospitals, and further supported by findings of a positive impact on breastfeeding (Thomas, 2008). 'Rooming in', also encouraged unrestricted contact between mothers and their infants as a means to promote bonding (Crouch and Manderson, 1995).

The work of Klaus and Kennell (1976) contributed significantly to the understanding of the importance of early mother-infant bonding. However, the validity of their findings was later questioned with much of the criticism being directed towards the methodology and interpretation of the study findings. In particular, it was unclear whether the women in the intervention group were aware or unaware of how they were managed. Further, the researchers did not state whether the observers were aware of each group's study allocation which could also have biased the result. Moreover, only half of the original number of women completed the study at one year, with no explanation of what had happened to the other women or why they were not followed up. Billings (1995), argued that the additional interest shown to women in the experimental group could have influenced their behaviour rather than the intervention in isolation. Other criticisms were that the generalisations made by Klaus and Kennell (1976) about the bonding behaviour of the mothers was weakened by

the small sample size of only 28 women, which was also biased in terms of the women's ethnicity, their social class and that they came from low income families (Myers, 1984, Eyer, 1994).

The concept that extended contact after birth was necessary to support the establishment of bonding was also criticised in later studies (Campbell and Taylor, 1979, Svejda et al., 1980). Svejda et al. (1980), completed a similar study to test the hypothesis that early and enhanced contact between mother and infant after birth facilitated bonding behaviour. Thirty primiparous lower-middle-class mothers with a healthy full term infant were randomly assigned to two groups. The intervention group women held their babies while on the labour ward for 15 minutes skin-to-skin contact, and for 45 minutes of additional contact in their hospital rooms. They were also encouraged to hold them every four hours for feeding and to keep them with them for 90 minutes prior to their being taken back to the nursery, instead of 30 minutes, which was usual hospital practice. Therefore, in the first 36 postpartum hours the intervention group mothers had approximately ten additional contact hours with their infants compared with the women in the control group. Spot checks were made by the researchers on the amount of time nurses spent with each study mother. In addition, the observers were blind to group status and trained to promote inter-observer reliability. All of the mothers and infants were videotaped at around 36 hours after delivery.

The observation period consisted of a 10 minute interaction and a 15 minute breastfeed. The researchers found that none of the behaviours of the mothers towards their infants differed between the two groups (Svejda et al., 1980). This was still a very small study which could not be generalized, although it was more robustly conducted. The researchers did not articulate if a power calculation was performed to ensure an appropriate sample size was recruited to be able to detect a difference in study outcomes. They also stated that the participants were randomly assigned into two groups but did not state how this was achieved. As such, the study failed to replicate Klaus and Kennell (1976) finding, which called into question the notion proposed by them that early or extended contact has an effect on maternal behaviour (Myers, 1984).

A longitudinal experimental study of 321 low-income mothers and infants examined the effects of two treatments (early and extended contact and home visits by a trained home visit worker recruited for the study purposes) (Siegel et al., 1980). Of the women recruited, 202 women who had a normal labour and birth with a healthy infant were randomly assigned into four groups: (1) both early and extended hospital contact and home visits by a trained home visit worker, (n=47); (2) early and extended hospital contact only (n=50); (3) home visit only, (n=53); and (4) routine hospital and follow-up care without early and extended contact or home visits (n=52).

Observations of maternal behaviour were made at four and twelve months, which included a 92-item attachment inventory and a 30-item behavioural list of a mother attachment inventory designed to describe maternal acceptance

versus rejection of the infant as well as involvement versus detachment (Siegel et al., 1980). Both scales were completed by two home observers after watching the mother bathing, dressing, feeding, and playing with their infant. Hospital and welfare agency records as well as interviews were used to determine the reporting of child abuse and neglect.

The study was of good quality in terms of methodology and approaches to data analysis, but the results showed that the two interventions were less important in explaining the differences between the two groups. The early and extended contact explained a significant but very modest (2% to 3%) amount of variance in maternal attachment scores at 4 and 12 months postnatal and was unrelated to abuse/neglect. In addition, the home visits were unrelated to any of the dependent measures. The researchers acknowledged that although their study supported the view that early and extended contact has a significant effect on mother-infant bonding, additional interventions are needed to support mother-infant attachment (Siegel et al., 1980).

Several authors have argued that a lack of evidence and inconsistent results do not support a “sensitive” or “critical” period immediately following birth, as proposed by Klaus and Kennell (1976), for the establishment of mother-to-infant bonding (Herbert et al., 1982, Lamb, 1982). Rather, it was suggested that maternal affections facilitating bonding between a mother and her infant did not occur at a specific period after birth. That is, the early hours and days after birth should be viewed as the beginning of a dialogue, whereby the growth of

reciprocal interactions with the baby develops progressively (Myers, 1984, Crouch and Manderson, 1995).

2.1.1 Definition of mother-infant bonding

As referred to earlier, there is no single standard definition of mother-infant bonding and there are disagreements between authors in terms of its components (Bicking Kinsey et al., 2014). The definition tends to vary depending on the perspective taken by the author, adding to the confusion surrounding its meaning. Some have described maternal infant bonding as having affective and behavioural components, such as emotional and physical behaviour (Feldman et al., 1999, Kennell and McGrath, 2005, Feldman and Eidelman, 2007). Figueiredo and Costa (2009), suggested that maternal bonding is related to a behavioural aspect, as well as a unique emotional and representational involvement, both being directed to keeping the necessary care and proximity for infant survival.

Others (Kumar, 1997, Else-Quest et al., 2003, Taylor et al., 2005, Bienfait et al., 2011, Gunning et al., 2011, Reay et al., 2011), have described mother-infant bonding as limited to an affective domain in the mother to infant relationship, (emotional components). In contrast, some authors (Cernadas et al., 2003, Levine et al., 2007, Noorlander et al., 2008) have described bonding in terms of behavioural components, such as gaze, touch and physical care of the infant. Previously Muller (1994) had described the mother-infant relationship as a unique affectionate relationship that develops between a mother and her

infant and persists over time. As well as affective and behavioural components of mother to infant bonding, (Feldman et al., 2007) included a biological association of mother- infant bonding, mainly regarding oxytocin. Jansen et al. (2008), proposed a definition of the maternal bond as a tie from mother to infant that promotes maternal behaviours aimed at mother to infant proximity and care giving. Subsequently, using a concept analysis, Altaweli and Roberts (2010) defined mother-infant bonding as a special, close relationship between the mother and her child that occurs during the sensitive period.

A recent review of maternal- infant bonding concepts highlighted that the many-sided definition of mother-infant bonding proposed by Klaus and Kennell (1976), which described maternal bonding as having affective and behavioural components, resulted in inconsistencies, as well as the blurring of boundaries between mother-infant bonding and other related concepts (Bicking Kinsey and Hupcey, 2013). Consequently, (Bicking Kinsey and Hupcey, 2013), proposed a theoretical definition of the concept of mother to infant bonding based on a well conducted recent systematic review of 44 studies: as a maternal driven process that occurs primarily throughout the first year of an infant's life but may continue throughout life.

The timing of the bonding process is another area reported with considerable variation by different researchers. For example, Silverman et al. (1993) referred to mother-to-infant bonding as a process that occurs in mammals during a sensitive period from a few hours to several days following birth. Karaçam and

Eroğlu (2003), measured time to bond in a cohort study of 100 women who had a normal vaginal birth in one Turkish hospital between 15 March 1999 and 6 April 2000. Women were recruited in birthing rooms and maternity wards postnatally before discharge home with follow-up conducted in the woman's home at 1, 3 and 12 weeks after labour. The study investigated the effect of episiotomy on mother to infant bonding. A first contact between the mother and her infant < 30 minutes was used as an indication of maternal bonding which implied that maternal bonding occurred at a specific time of < 30 minutes post-delivery. Although the quality of this study is poor, it highlights the variations in how mother-infant bonding is reported.

Other researchers (Taylor et al., 2005, Reck et al., 2006, Feldman and Eidelman, 2007, van Bussel et al., 2010b, O'Higgins et al., 2013) have examined maternal infant bonding in the first year of life, describing it as a process that occurs over an extended period of time.

There are also disagreements among researchers on the process of mother-infant bonding. Taylor et al. (2005) and O'Higgins et al. (2013) described maternal bonding as a mother's feeling towards her infant which does not require a response of any kind from the infant. In contrast, Brockington (2008) and Figueiredo and Costa (2009) suggested that maternal bonding is a bi-directional process in which the infant participates in the bonding process, proposing that certain infant behaviours are strong social factors that elicit a mother's response.

2.1.2 Facilitating mother-infant bonding

2.1.2.1 Breastfeeding

Breastfeeding is often mentioned in literature as a positive factor to promote mother-infant bonding (Dieterich et al., 2013). However, this positive effect of breastfeeding on the mother-infant bonding is often assumed with no empirical evidence to support the assumption (Leung and Sauve, 2005, Jansen et al., 2008, Altaweli and Roberts, 2010, Okeh, 2010, Liu et al., 2013). Most of the studies identified for this review assessed mother-infant bonding by observation of maternal behaviour and interaction during infant feeding, which is only one aspect of mother-infant relationship. However, there has been little research investigating the role of breastfeeding on mother-infant bonding (described as maternal feeling towards her infant rather than mother-infant interaction) and the few studies that have done so reported no association with breastfeeding (Edhborg et al., 2005, Bicking Kinsey et al., 2014).

Cernadas et al. (2003) in an observational study of 597 mothers examined the effects of maternal bonding on breastfeeding duration rather than on the quality of breastfeeding on maternal bonding to her infant. In this study, participants were interviewed monthly by telephone about how they fed their infants. At six months postnatal, mother-infant bonding was assessed at home, with maternal-infant interaction observed during breast feeding. Observations were recorded on the frequency of maternal gaze on the baby and how attentive the mother was to her infant's needs as well as how often the mother caressed her infant during breastfeeding. The study found that a longer duration of exclusive

breastfeeding was associated with better mother-infant bonding during the first six months after birth.

Other studies examined reasons why mothers choose to breastfeed their infants. These studies most often reported better bond formation through breastfeeding as the reason to commence breastfeeding (Arora et al., 2000, Gijsbers et al., 2005). Studies that used videotaping to explore mother-infant interaction during breastfeeding have reported that breastfeeding mother-infant dyads spend more time in a mutual gaze during feeding than bottle-feeding dyads (Wiesenfeld et al., 1985, Lavelli and Poli, 1998). However, Brandt et al. (1998) reported better mother-infant interaction during the first days postpartum and a higher frequency of breastfeeding at six weeks. A more recent Canadian study of seventy-seven mother-infant dyads also found better mother-infant interaction in breastfeeding mothers compared to non-breastfeeding mothers (Bigelow et al., 2014).

A large prospective cohort study of 543 participants in the USA, asked participants to complete a home interview and complete a postal questionnaire regarding infant feeding (Else-Quest et al., 2003). Mother-infant interaction was observed at four and 12 months postpartum in women who had breastfed for at least a week (n=439) and compared with women who had not initiated breastfeeding (n=94). In a face to face interview in the participants' own homes at four months postpartum, women were asked questions regarding infant feeding practices in the first week postpartum. They were videotaped for three minutes during a feeding session after the interview. At 12 months postpartum,

they were videotaped again, this time for five minutes while reading a book to their infants. The researchers found that mothers who had breastfed for at least one week showed higher-quality interactions with their babies at four months, but not at twelve months postpartum (Else-Quest et al., 2003). The researchers concluded that mothers may benefit from breastfeeding by feeling stronger bonds in the early postpartum months, but such benefits are absent by the first birthday, thus suggesting that the breastfeeding effects on maternal bonding are short-term.

Although this study attempted to support the positive effect of breastfeeding on mother-infant interaction using a large sample size, methodological limitations need to be highlighted: There was a possibility of reporting bias as information on breastfeeding was reported retrospectively. Moreover, the authors did not mention if the women breastfed exclusively and did not report method of infant feeding at four or 12 months when recording mother-infant interaction, as measuring these variables may have provided more conclusive evidence of an association. Additionally, the study reported significant group differences in the level of maternal education; breastfeeding mothers were more educated than the bottle-feeding mothers, which could account for better mother-infant interaction.

Else-Quest et al. (2003), acknowledged that the physiological processes that could account for the effect of breastfeeding on mother-to-infant bonding might operate through the nipple stimulation that the infant provides when sucking, which triggers an oxytocin surge in the mother. Oxytocin is associated with the milk let-down reflex, which results in the expression of breast milk. Breastfeeding also provides increased skin-to-skin contact for the mother-infant

dyad. When mothers hold their nude infants against their chests in this way, increases in maternal response to the infant and bonding are observed (Anderson, 1995, Tessier et al., 1998).

Despite the assumption that breastfeeding promotes maternal bonding in some literature the findings of a systematic review by Jansen et al. (2008) contradicted these claims. Of 41 papers included in the review, 22 made a general statement on the positive effect of breastfeeding on any aspect of the mother-infant relationship without any reference to empirical studies to support this claim. Thirteen papers examined reasons why women choose to breastfeed, which was most often to be able to bond with their infant. However a reason to choose breastfeeding is not the same as the effect of breastfeeding on mother-infant relationship. Only six papers directly examined the association between breastfeeding and mother-infant relationship, three of which examined mother-infant bonding while the other three examined infant-mother attachment. The review highlighted the lack of evidence on the effect of breastfeeding on the quality of mother-infant bonding.

Jansen et al. (2008) indicated that the theoretical mechanisms through which breastfeeding may enhance the mother-infant bonding (i.e. endocrine and sensory factors involved in breastfeeding) can be found in human and animal studies, but the empirical studies reviewed did not provide convincing evidence of this. The review findings was supported by (Hahn-Holbrook et al., 2013) who suggested that despite the conventional belief that breastfeeding helps mothers

bond with their babies there was no evidence that this is the case. However, breastfeeding may provide an extra incentive for mothers who are reluctant in that role or are experiencing challenges to care for their infants, but it is not necessary for maternal bonding to occur as adoptive mothers or mothers who bottle-fed can bond equally well with their infants (Holbrook et al., 2013).

2.1.2.2 Maternal social support

It has been suggested that a woman's social network may serve as a protective function in her relationship with her new infant. This may help with child care tasks and provide a source of emotional support, an important aspect of this protective function (Adler et al., 1991). An earlier study also proposed the benefit of social support to enhance mother-infant bonding (Anisfeld and Lipper, 1983). However, the focus of maternal support and mother-infant bonding has been limited to doula and midwife continuous support during labour (Sevil and Coban, 2005, Ekström and Nissen, 2006, Altaweli and Roberts, 2010). An extensive literature search prior to starting the current study did not identify any previous research that had specifically studied the effect of maternal support on mother-infant bonding defined as maternal affectionate feelings towards her infant. However, while updating this literature review, a relevant more recent study was identified (Bicking Kinsey et al., 2014) which specifically examined maternal social environment and mother-infant bonding during the postnatal period, as part of a large prospective cohort study of 3005 women recruited for the First Baby Study in Pennsylvania USA. Participants were interviewed during their third trimester of pregnancy and at one year postpartum. The authors used a modified version of The MOS social support survey (Sherbourne and Stewart,

1991) and included items specifically related to social support that a new mother would need. The study also used a six-item scale developed by the research team to assess partner baby support. A ten item shorten version of The Postpartum Bonding Questionnaire (Brockington et al., 2001) was used to assess maternal-infant bonding.

Study findings confirmed the positive effect of maternal support on mother-infant bonding. This was a good quality study in terms of study design and use of scales which had acceptable internal reliability (Cronbach's alpha between 0.73- 0.88), but there were some limitations that needed to be highlighted. Study participants were older, more educated and mostly non-Hispanic White women, making the study difficult to generalise to other populations.

Conversely, substantial literature exists on the positive effect of social support on mother–infant interaction, which differs from maternal affection towards infants (the main focus of the current study). An increase in the father's involvement and a degree of marital emotional support for the woman has been associated with a reduction in maternal intrusiveness in face to face interaction and a high maternal reactivity/sensitivity during interaction with the infant (Feldman et al., 1997, Pauli-Pott et al., 2003) . Similarly, among women living in adverse conditions, such as poor housing and financial insecurity, the presence of the partner in the home and the level of practical support from them have proved to be helpful and produced maternal sensitivity in their face to face interaction with two month old infants (Cooper et al., 2009). Although the marital relationship is often considered as the most important source of social

support for the woman, other relatives and friends are also regarded as important providers of maternal social support (Gelfand et al., 1992, Cooper et al., 2009, Leahy-Warren et al., 2012).

2.1.3 Impaired mother-infant bonding

Despite the fact that most women experience affection for their infant at birth, the onset of maternal affection may be delayed in some women (Robson and Kumar, 1980). More recent studies have also shown a progressive nature of mother-infant bonding (Edhborg et al., 2005, van Bussel et al., 2010b, Yoshida et al., 2012). As explained earlier, a delay in maternal affection may be normal for some women, but problems may arise when the delay progresses and a woman is expressing negative or lack of feelings towards her infant, described as mother-infant bonding disorder (Brockington, 1996, Kumar, 1997).

Robson and Kumar (1980) in a seminal paper derived from a study of 185 women recruited in one London teaching hospital showed that up to 40% of first time mothers and 25% of multiparous mothers were indifferent to their babies on first holding them. The results were obtained from three separate samples: 104 primiparous women followed through pregnancy and their first postnatal year, and two subsidiary samples of 41 primiparous and 40 multiparous women who were only studied after they had given birth. A semi-structured questionnaire was administered to all women on the seventh day after delivery, which included questions on the women's perceptions of their labour and birth, their feelings for the babies when they first held them and at the time of

interview. Forty three women from sample one were rated as having felt indifferent about their babies, 13 mothers experienced mixed feelings and 48 clearly recalled immediate affection. In the second group, 16 primiparous women recalled initial feelings of indifference or dislike for their babies and 10 multiparous women recalled similar initial feelings. The study also found that although women's emotional reactions when they first held their babies were predominantly indifferent, most developed affection within the first week of delivery. Moreover, after three months, a woman was likely to show dislike or indifference towards her baby if she was clinically depressed.

Robson and Kumar 1980's study was the first in this field of research and their findings made an important contribution to knowledge of delayed onset of maternal affection after childbirth. However, methodological shortcomings are important to highlight: the purpose of the study was not clearly stated; there was no clear research question or hypothesis described by the authors and the research processes were not clearly described. In addition, some participants were recruited during pregnancy and others postpartum, but the authors did not explain why this approach was used or what types of data were collected on the women recruited. Furthermore, the authors did not screen for psychiatric disorders or exclude mayor obstetric complications, which could have contributed to the high prevalence of delayed maternal affection noted on first time mothers (Wittkowski et al., 2007).

In a subsequent paper, Kumar (1997) published a study of 44 self-selected women who responded to an advert placed in the newsletter of the Association for Postnatal Illness, a national voluntary support organisation for mothers suffering from postnatal psychiatric problems. The newsletters were sent to 800 volunteers who had previously experienced postnatal mental illnesses. Fifty-three responded, but only 49 whose replies indicated a possible relationship problem with at least one of their babies were sent a questionnaire. All 49 women completed the questionnaire, but five women were excluded as their responses did not indicate relationship problems with any of their children. Of the 44 respondents included in the analyses, 29 had one child; the remainder had two or more children.

Participants completed a questionnaire about their feelings after the birth, changes over time and their current feelings in relation to each of their children. They gave detailed accounts of absent affection, hate, rejection, neglect or impulses to harm. These emotional and behavioural reactions were specific to one child (Kumar, 1997). The author claimed this to be evidence for a disorder of mother–infant bonding.

Although the importance of recognising this disorder was highlighted, findings could not be generalised due to the low response rate and factors other than postnatal psychiatric illness, such as ethnicity, sex of the baby and social support, which could have contributed to negative maternal affections towards the baby, but were not considered. There was also possible selection or recall bias because the women were self-selected and the reported negative feelings

towards their infants were based on the recollection of their feelings as far back as when they had their first baby, which may have been some years previously.

A retrospective case note survey of 200 women reported that the disorder of mother-infant relationship was found in around a quarter of mothers referred for psychiatric help to a Mother and Baby Unit, Birmingham, UK using a report from in-patient nursing observation records (Brockington, 1996). Further research by the same team (Brockington, 2006) assessed the frequency of severe disorder of the mother-to-infant relationship in 206 women referred to mental health services in Birmingham, the UK and Christchurch, New Zealand. They reported that 11% of women had established rejection of their infant, 15% had threatened rejection, while 28.6% had various degrees of pathological anger, which was severe in 8.3% of the women. The assessment was an interview conducted by the lead author using the Birmingham Interview for Maternal Health (Brockington, 2006). The ages of the infants at the time of assessment ranged from 5 to 52 weeks with a mean age of 26 weeks. Brockington (2011) suggested that the referral rate to specialized units in Britain and New Zealand, where the 2006 study was conducted, was about 5% among mothers who had recently given birth and hence proposed a 1% prevalence of mother-infant bonding relationship disorder in the general population.

A study in Hong Kong recruited 62 women diagnosed with postpartum depression from the Perinatal Specialist Out-patient Psychiatrist Clinic (Siu et al., 2010) to assess impairment of mother-infant relationship among those with

infants under one year. Participants were interviewed using the fifth edition of the Birmingham interview (Brockington, 2006) and were asked to complete the Chinese version of the postpartum bonding questionnaire (Siu et al., 2010). The study found that 24% of participants had impaired bonding while 8% had established rejection of their infant, but the study had several limitations. The researchers did not measure variables other than postnatal depression that could be confounding factors for impaired mother-infant bonding and did not report the minimal age of the infants, making it difficult to comprehend their results, especially the prevalence rate. In addition, researchers did not include the number of women approached to participate or the overall response rate.

Klier (2006), presented two case reports of disturbed mother–infant bonding following assessment of the women using the postpartum bonding questionnaire (Brockington et al., 2001). In the first case, a mother with postnatal depression described feelings of guilt and obsessional thoughts about harming her 7 day old infant (e.g. a feeling that her child would disappear and she would not care for it anymore). A second mother with postnatal depression, who had a severe bonding disorder with her twins, felt extreme anger when her infants cried, and wished '*that someone would take them away*' (Klier, 2006 p. 290). Brockington et al. (2006) proposed four factors for this disorder, which are presented in table 2.1.

Table 2-1 Four factors of impaired mother infant relationship disorder

Mild disorder	The mother experiences delay in the onset or loss of the maternal emotional response to her infant.
Infant focus anxiety	This could be mild or severe: mild, the mother reports feeling anxious when left alone with her infant and severe, when the anxiety leads to reduced contact with the infant.
Pathological anger	This could be mild, moderate or severe anger towards the infant, with lattermost referring to when the mother has lost verbal control and shouts and/or swears at the infant
Maternal rejection	The rejection could be either threatened (when the mother lacks a positive of maternal emotional response to her infant and has a wish to relinquish the care of the child temporarily) or established rejection (when the mother expresses strong negative feelings about the child, such as dislike, hatred and/or regret about the birth.

(Brockington 2006, p. 250).

It is important to note that although Brockington et al. (2006) proposed the above criteria of the mother-to-infant relationship disorder, the severity of these disorders, especially pathological anger and rejection, are not the focus of the current study. Rather the study is focusing on the mild disorder where the mother experiences a lack of emotional affectionate response to her infant.

2.1.4 Factors associated with poor mother-infant bonding

Many factors have been reported to be associated with bonding difficulties including: unwanted pregnancy, infant temperament, unfortunate events at the time of childbirth, the mother's health and psychological adjustment, especially

postnatal depression, and the social environment in which the pregnancy, birth, and early interactional processes occur (Marks et al., 1992, Kumar, 1997, Brockington, 2004, Bicking Kinsey and Hupcey, 2013). A Portuguese study found that poor mother to infant bonding was significantly predicted when the woman was depressed and had a lower educational level. Unemployment and being single was also associated with negative emotions toward the infant (Figueiredo and Costa, 2009).

2.1.4.1 Maternal mental health

Women may experience a range of mental health problems during pregnancy and the postnatal period, including anxiety, depression, transient psychological problems (i.e. the blues) and in very rare cases, psychosis (Gavin et al., 2005). A systematic review looking at the risk factors for depressive symptoms during pregnancy evaluated 57 studies and found that maternal anxiety, life stress, history of depression, lack of social support, unintended pregnancy, domestic violence, lower income, lower education, single status, and poor relationship quality were associated with antenatal depression (Lancaster et al., 2010).

There is now considerable research into the negative impact of maternal mood disturbance or stress levels during pregnancy on fetal development and infant outcome, which are thought to induce long-term and persistent effects on the child (O'Donnell et al., 2009b, Schetter and Tanner, 2012, Glover, 2014, O'Connor et al., 2014) i.e. symptoms of attention deficit hyperactive disorder, greater levels of anxiety, temperament and behavioural problems (Field, 2010, Tegethoff et al., 2011, Grzeskowiak et al., 2012, O'Donnell et al., 2014).

Antenatal depression and anxiety are viewed as the most important risk factors for postnatal depression (Terry et al., 1996, Da Costa et al., 2000, Alder et al., 2007, Olhaberry et al., 2013), which in turn is viewed as a major risk factor affecting the development of the mother-infant relationship (Kumar, 1997, Brockington, 2004).

2.1.4.2 Postnatal depression

Postnatal depression is defined as a non-psychotic depressive episode meeting the standardised diagnostic criteria for a minor or major depressive disorder, according to *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)*, (American Psychiatric Association 1994), beginning in or extending into the postnatal period (Cox and Holden, 2003, Logsdon et al., 2006, Brealey et al., 2010). It is differentiated from the postpartum blues, a mild transient and predictable mood disturbance that often occurs three to five days postnatally (Buttner et al., 2012). It is also distinguished from postpartum psychosis, a rare acute psychotic episode that often begins within the first two to four weeks after delivery (Sit et al., 2006).

The prevalence of postnatal depression has been described as ranging from 13% to 19% (Gavin et al., 2005, Mann et al., 2010, O'Hara and McCabe, 2013). This wide range reflects the populations sampled, timing of assessment, criteria for inclusion of a 'case', assessment and diagnostic measures used as well as the methodological quality of studies (Gavin et al., 2005, Dennis and Hodnett, 2007). A systematic review by Mann et al. (2010) claimed that knowledge of the prevalence and incidence of postnatal depression in the first postnatal year was

poor due to limited generalisable evidence in the form of high quality systematic reviews, because of the issues of study design and quality. Moreover, it has been suggested that accurate figures are lacking owing to under-reporting of symptoms of depression by women as well as under-identification by health care professionals (Nielsen et al., 2000, Yonkers et al., 2001).

Several studies have reported an association between postnatal depression and poor bonding (Brockington, 1997, Kumar, 1997, Taylor et al., 2005), possibly because the former affects a woman's ability to cope with the care of her baby, and hence limits her capacity to engage positively with the child in social interactions (Murray et al., 2003, Logsdon et al., 2006). Some studies have identified mother-to-infant interaction as a mediator of adverse effects on children of postnatal depressed mothers (i.e. long term emotional and cognitive development of the infant) (Murray et al., 1996, Beck, 1998, Bornstein et al., 2012). Other work has suggested that children of mothers who have experienced postnatal depression are more likely to show elevated rates of behavioural, attention and interpersonal disturbances, outlasting the maternal depressive episode throughout childhood (Murray and Cooper, 1997, Hay et al., 2001, Righetti-Veltema et al., 2002) . In a meta-analysis of nine studies, (Beck, 1995) reported that postpartum depression has a moderate to large adverse effect on maternal-to-infant interaction in the first year of birth. Furthermore, postnatally depressed mothers have been shown to be less sensitive when interacting with their infants than control mothers who had no postnatal depression (Campbell et al., 2004, Field, 2010, Murray et al., 2010).

In a longitudinal cohort study of 101 mother-to-infant pairs in Germany, Moehler et al. (2006) examined whether maternal-infant bonding was impaired by maternal depressive symptoms. Mother-to-infant bonding was assessed using the Postpartum Bonding Questionnaire (PBQ) (Brockington et al., 2001), while women potentially experiencing postnatal depression were assessed using the EPDS scale (Cox et al., 1987) at two weeks, six weeks and four months and fourteen months postpartum. The study found that maternal depressive symptoms at two weeks, six weeks and four months postnatally were associated with lower quality of maternal bonding with the infant from two weeks until fourteen months of age. Even mild maternal depressive symptoms had a significant impact on maternal bonding, if they occurred during the first four months of life.

Moehler et al. (2006), argued that the potential link between postnatal depression and mother-infant bonding should be investigated further because symptoms of poor maternal bonding are linked to impaired mother-infant interaction, infant and toddler attachment as well as childhood behaviour and development. The methodology of this study was robust, with the authors clearly outlining the rationale in relation to the importance of the study. A research hypothesis was defined, and study sample size and the power calculation were also reported. A limitation was that the researchers used a non-probability convenience sample of women who volunteered, which may have affected the study's external validity.

Some studies have investigated the effect of postnatal depression on mother-to-infant bonding (e.g. Kumar, 1997; Taylor et al., 2005; Moehler et al., 2006), although few researchers have considered the effect of antenatal anxiety and

depression on mother-to-infant bonding. A Portuguese study conducted with 91 first time mothers examined the effect of a mother's antenatal anxiety, depression and emotional involvement with her infant both before and after childbirth. It reported that maternal depression predicted worse emotional involvement before the birth, while anxiety predicted a worse emotional involvement with the infant following the birth (Figueiredo and Costa, 2009). This study was the first to link maternal antenatal anxiety with mother-infant bonding, although there were some methodological issues. The authors reported that participants were randomly-selected from an obstetric outpatient hospital unit and 90% of the women agreed to take part in the study, but did not provide details on how many women were approached or recruited. In addition, the authors did not report if a power calculation was conducted to ensure an appropriate sample size was achieved. The researchers used the Edinburgh Postnatal Depression Scale (EPDS) with a cut-off of ≥ 10 EPDS instead of the more usual $\geq 12/13$ to detect women who may be at risk of experiencing depression (Cox et al., 1987) and as a consequence, may have included women who were not at risk of depression.

The researchers also used a modified Mother Infant Bonding Scale (MIBS) (Taylor et al., 2005) to assess mother to infant bonding and added three more items to the original scale. However, they used a score of ≥ 1 to confirm negative bonding rather than ≥ 3 as recommended in the original study, increasing the possibility of false positives. The reliability of their modified version has not been tested in other research except by members the same research team. Although internal consistency was reported (alpha of Cronbach's=0.61) with the original version of the bonding score, a reliability

score of 0.70 or higher has been suggested as appropriate when using a psychometric instrument (Choudhury, 2010). Despite these studies, gaps remain in the knowledge of the association between antenatal depression and anxiety and mother-to-infant bonding.

In summary, this section has included an overview of the concept and definition of mother-infant bonding. The definitions of impaired mother-infant bonding and factors that promote or hinder bonding have also been discussed. Breastfeeding and social support have been explored as mediators for maternal bonding, but the evidence to support findings is limited. In addition, maternal mental health problems, in particular postnatal depression has emerged as strongly associated with impaired mother-infant bonding. In fact, most studies reviewed on impaired mother-infant bonding have focused on women with mental health problems, with a high incidence of impaired bonding reported.

As the aim of this study was to investigate antenatal predictors of poor mother-infant bonding in a non-clinical perinatal population which met study inclusion criteria, it was considered important to further explore the relevant literature to ensure these evidence 'gaps' were met in order to 'frame' the current study. The findings of the next phase of the literature review are presented in the following section.

A non-clinical perinatal population refers to pregnant women in the current study who had no known history of mental health problem at time of recruitment.

2.2 Structured literature review

2.2.1 Introduction

The aims of this literature review were to: 1) determine current evidence on the rates of impaired mother-infant bonding in women with no known diagnosis of mental health problems and 2) critically review studies designed to measure psychosocial and obstetric factors associated with early mother-infant bonding disorder.

2.2.2 Methods

To examine the rate and psychosocial factors associated with impaired mother-infant bonding in women with no known diagnosis of mental health problems, two specific review questions are developed:

- *What is the rate of early mother-infant bonding disorder in a non-clinical perinatal population?*
- *What psychosocial and obstetric factors are associated with early mother-infant bonding disorder in this population?*

2.2.2.1 Search strategy

Several electronic databases were systematically searched to identify studies considered relevant for this review. As randomised control trials (RCT) would not be ethically possible with these groups of women given the nature of subject being studied, the review was developed to identify other quantitative studies, including observational studies. The databases searched included: MEDLINE, Maternity and Infant Care, PsycINFO, EMBASE, PubMed, Science Direct, SciVerse Scopus, Web of Knowledge, Web of Science, and British Nursing Index (BNI). Additionally, the Archives of Women's Mental Health electronic journal were searched as it is regarded as a premier resource for all aspects of

psychiatric and psychosomatic disorders in women during the perinatal period. The search strategy was developed in consultation with Nursing and Midwifery Information Specialists from Kings College London. A systematic approach to the literature search was used, search terms included: “mother-infant attachment”, “mother-infant bonding”, mother-infant relationship”, “bonding disorder”, “bonding failure”, “and impaired bonding”. Keywords were searched in combination with search terms, which included: “antenatal”, “antepartum”, “anxiety”, “bonding”, and “depression”, “postnatal”, and “postpartum”, pregnancy. Subject headings e.g. (Medical Subject Heading (MeSH) and free-text terms were used to maximize the sensitivity of the search.

The dates searched were from January 1980 to August 2013 and updated in September 2014. Only studies published in English language were included due to lack of resources and time constraints to obtain translation of any identified papers. The dates were selected because the first study of delay or lack of maternal affection to her infant was first published during the 1980s, (Robson and Kumar, 1980). The following inclusion and exclusion criteria were used.

2.2.2.2 Inclusion criteria

- Studies which measured the early emotional bond or relationship using a validated self-rating questionnaire.
- Studies of impaired mother-infant bonding assessed from birth and up to 1 year postpartum.
- Studies that recruited women from maternity units or community settings
- Studies published in English

2.2.2.3 Exclusion criteria

- Studies that assessed impaired mother-to-infant bonding more than 1 year postpartum
- Studies that assessed mother to infant bonding using mother–baby interaction scales
- Assessment of impaired mother to infant bonding in women recruited from mother and baby or psychiatric units
- Non-English language studies.

2.2.3 Search results

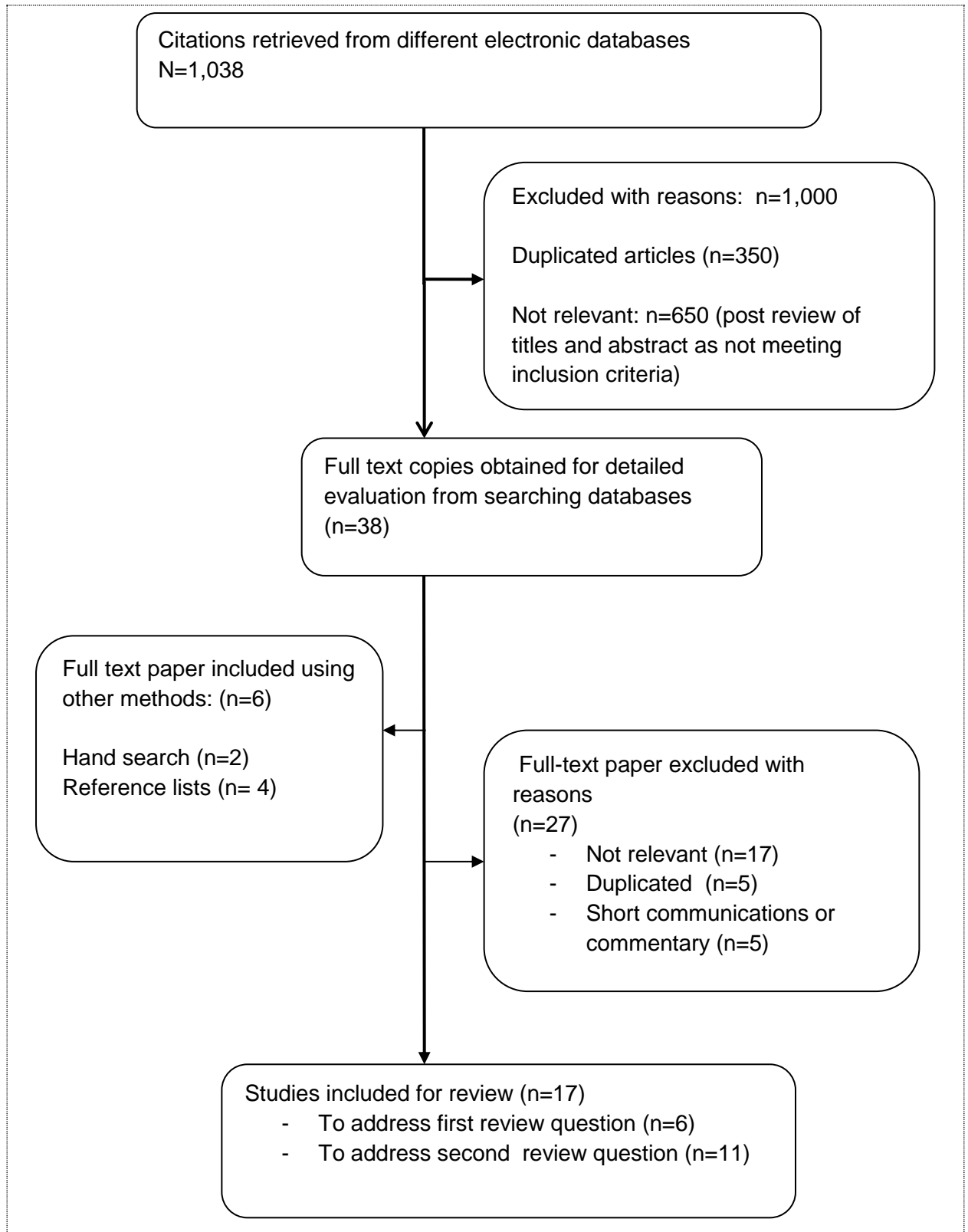
The literature search identified 1,038 articles which matched pre-specified search terms, with around 350 excluded after they were identified as duplicates of the different databases searches. A further 650 articles were excluded as not relevant after their abstracts were read by the researcher. Full text versions were obtained for 38 studies. The reference lists of all relevant papers were hand searched to identify further studies for possible review that may have been missed.

A further six studies were obtained, two following a hand search of relevant literature and four identified from the reference lists of selected studies; 27 studies were excluded after an in-depth review of abstracts owing to reasons such as the assessment of impaired mother-infant bonding involving women recruited in mother and baby units or psychiatric units, an exclusion criteria for this review. Studies measuring mother-to-infant bonding or relationship after one year postpartum or use of an unvalidated mother-to-infant bonding scale were also excluded. If a publication was duplicated, a commentary or short communication rather than a primary research paper, it was also excluded.

2.2.3.1 Selection of studies

After reviewing the titles and abstracts of all identified studies, full texts were obtained and screened. After exclusion of studies considered not relevant or where a full text version of the work was not available, the remainder were considered appropriate for further examination. A flow chart of the eligible studies and stages when a study was excluded is presented in Figure 2.1.

Figure 2-1 Flow diagram of the literature identification and selection process



2.2.4 Overview of reviewed studies

A total of 17 observational studies were selected for review. Six studies addressed the first review question namely: What is the rate of early mother-infant bonding disorder in non-clinical perinatal population? Eleven studies addressed the second review question, namely: What psychosocial and obstetric factors are associated with early mother-infant bonding disorder in this population?

2.2.4.1 Prevalence of impaired mother-infant bonding in non-clinical perinatal population

Rates of poor mother-infant bonding were reported in six out of seventeen studies reviewed. Five were undertaken in high income countries, including France (Bienfait et al., 2011), Germany (Reck et al., 2006), Portugal (Figueiredo et al., 2009), Sweden (Edhborg et al., 2005) and the United Kingdom (Taylor et al., 2005). The sixth study originated from a low income country, Bangladesh, (Edhborg et al., 2011). The sample sizes of these studies ranged from 78 (Bienfait et al., 2011) to 872 (Reck et al., 2006). The mean maternal age of women in the six studies was 30 (range=25-33 years). Infant age at time of assessment of impaired mother-infant bonding was between two days to three months old. Data were collected either through a maternal self-completed questionnaire (PBQ, 2001; MIBS, 2005), or a combination of a self-rating questionnaire and clinical interview using the fifth edition of the Birmingham Interview for Maternal Mental Health (Brockington et al., 2006).

Taylor et al. (2005) reported a rate of 8.9% of poor bonding in a study of 144 women who were 12 weeks post-delivery. Based on data from the study by Taylor et al (2005), an eight item self-rating question was developed, which was subsequently used to assess impaired mother-infant bonding in the early postnatal period in several studies (Wittkowski et al., 2007, Figueiredo et al., 2009, van Bussel et al., 2010b, Bienfait et al., 2011). However, the study by Taylor et al (2005) had some limitations in that it did not describe the ethnicity of study participants and only included women who had a vaginal delivery; an important issue as mode of birth, especially emergency caesarean section and instrumental delivery have been associated with impaired mother-infant bonding (Bicking Kinsey and Hupcey, 2013). Hence, rates reported may not be representative of the population studied, with no account taken of other potential confounding factors associated with impaired bonding, such as poor social support, unwanted pregnancy and level of education (Brockington, 2008).

Figueiredo et al. (2007)) compared the rate of impaired bonding between women and their partners (father of the baby) in a Portuguese study, with bonding assessed using the Mother Infant Bonding Scale at two time-points, 24 and 48 hours post birth, in a sample of 150 mothers and 141 fathers. The researchers reported a rate of 4% impaired bonding in the mothers and a lower rate of 3% in their partners. A longitudinal prospective study by Reck et al. (2006) from Germany reported a rate of 7.1% of impaired bonding. Participants were recruited in an inpatient delivery unit of a maternity hospital and mother-infant bonding was assessed using the German version of the Postpartum Bonding Questionnaire (PBQ), (Brockington et al., 2001) with a sample of 862

women two weeks post-delivery. Despite the comprehensiveness of this study and the use of a large sample size, limitations included a lack of a clear explanation of how the cohort was recruited and the study response rate was not reported. Only German speaking women were recruited.

Bienfait et al. (2011) reported a rate of 13% of impaired mother-infant bonding in 78 women based on clinical interviews by a paediatric psychiatrist, using a semi-structured question on maternal feeling for their infants. Their study was conducted in neonatal units of a maternity ward in a university hospital in France. Women who were inpatients on a postnatal ward, whose infants were in the neonatal unit, were recruited 48 hours after birth. A wide variety of reasons for women being admitted were reported, including premature birth (34–37 weeks gestation), giving birth to a baby with a low infant birth weight (between 1800g and 2200g), suspected maternal–fetal infection, a previous psychiatric history or psychological vulnerability, prevention of weaning syndrome from maternal illicit drug intake during pregnancy, complicated medical situation and exclusive maternal breastfeeding. Women completed self-report questionnaires of impaired mother-infant bonding using the Mother-to-Infant Bonding Scale (MIBS) 48 hours post birth.

Although the study determined the threshold value for MIBS through inclusion of a clinical interview, opportunistic recruitment of a diverse sample of women admitted to the postnatal ward may have introduced selection and reporting bias. For example, those admitted with psychiatric history or psychological vulnerabilities may have reported an increased rate of poor bonding disorder

(Brockington et al., 2006). It does not appear that the authors adjusted for possible confounding factors, such as socio-demographic background (e.g. marital status and education) in their analysis, in line with other studies (Figueiredo et al., 2007, Edhborg et al., 2011).

2.2.4.2 Psychosocial factors associated with impaired mother-infant bonding

Twelve studies were reviewed of which nine were prospective cohort studies and three cross sectional ones. They all originated from high income countries, including Belgium, France, Germany, Japan, Portugal, Sweden, the United Kingdom and the USA. The majority of participants were women of white ethnic origin (with only two reporting the inclusion of women from other ethnic groups, Muzik et al. 2013; O'Higgins et al., 2013). Women were recruited from hospital antenatal clinics, postnatal wards, or community-based cohorts between the third trimester of pregnancy or first week postnatal. Only one study recruited women at four months postnatal. Sample sizes varied between 64 (Gunning et al., 2011) and 862 (Reck et al., 2006).

Five studies examined an association between maternal depressive symptoms and impaired mother-infant bonding (Edhborg et al., 2005, 2011; Moehler et al., 2006; O'Higgins et al., 2013; Reck et al., 2006). Studies examining the reliability and validity of the MIBQ also reported relevant data (Bienfait et al., 2011; Taylor et al., 2005; VanBussel et al., 2010; Wittkowski et al., 2007; Yoshida et al., 2012). Figueiredo et al. (2009) and Muzik et al. (2013) examined other factors or predictors of impaired mother-to-infant bonding, including socio-demographic

characteristics, previous life events, and early experience with infant and infant characteristics. Two studies examined different aspects namely, if maternal self-reported attachment anxiety and avoidance were related to a maternal bonding problem (Gunning, 2011) and the influence of antenatal ruminative thinking on the early mother to infant relationship (Muller et al., 2013). In one study (Kokubu et al. 2012), the study aim was not specified.

All of the studies used maternal self-report to obtain data on maternal bonding with variations in measures used. Seven (Bienfait et al., 2011; Figueiredo and Costa, 2009; Figueiredo et al., 2009; Kokubu et al., 2012; O'Higgins et al., 2013; Taylor et al., 2005; Yoshida et al., 2012) used the original or a translated version of the MIBS developed by Taylor et al. (2005). Seven (Edhborg et al., 2005; 2011; Gunning et al., 2011; Moehler et al., 2006; Muller et al., 2013; Muzik et al., 2003; Reck et al., 2006) employed a translated or the original version of the PBQ, developed by Brockington et al. (2001). The other two studies (VanBussel et al., 2010; Wittkowski et al., 2007) used both questionnaires to assess impaired mother to infant bonding. There were also variations in the ages of the infants when bonding was assessed, ranging from two days to one year postpartum. Consequently, there was a possibility of detection bias as assessment carried out very early, e.g. 2 days postpartum, may not accurately reflect maternal bonding difficulty. This is an important consideration with increasing evidence that women who may not feel immediate affection towards their baby could do so later (Robson and Kumar, 1980; Taylor et al., 2005; Wittkowski et al., 2007; Yoshida et al., 2012).

2.2.5 Methodological quality of the reviewed studies

The Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement (von Elm et al., 2007) was used to assess the quality of reporting observational studies (see appendix 1). Although STROBE is not a tool for assessing the quality of primary studies, it provides a useful indication of the essential information needed to appraise the conduct of primary studies (Sanderson et al., 2007). Assessment of methodological quality of each selected study was then performed using the detailed questions in the Critical Appraisal Skills Programme checklists for observational study (CASP); (Singh, 2013), (see appendix 2).

Overall the methodological quality of nine of the 17 selected studies was weak, seven were moderate and one was strong when assessed against CASP criteria (see table 2.2). There was a lack of clear definition of impaired mother to infant bonding, poor representativeness and very limited generalisability across the studies. All studies excluded participants on the basis of language; most women in the studies were white except for that of Edhborg et al. (2011), who recruited women from Bangladesh and two others who reported other ethnicities in their sample, Muzik et al. (2013) (African American, 19%) and O'Higgins et al. (2013) (black 10% and other ethnicities 10%). There was a possibility of selection bias in some studies as only groups expected to be at a higher risk of the outcome of interest were recruited. For example, Gunning et al. (2011) recruited women of low economic background, Muzik et al. (2013) targeted women with a history of child abuse and O'Higgins et al. (2013) had sample overrepresented with women who had postnatal depression. Only two

studies (Edhborg et al., 2011; Moehler et al., 2006) reported power calculations and response rates also varied between studies (31%-98%). Attrition bias was discussed in only three studies (van Bussel et al., 2010b, Muzik et al., 2013, O'Higgins et al., 2013) but not in others.

Table 2-2 Characteristics, findings and quality of reviewed studies

	Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
1	Bienfait et al. (2011) France	Prospective cohort Study. N=78 Setting: neonatal unit of a maternity ward	48 hours post delivery Measures: 4 self-rating questionnaire and face-to-face interview. Mother-infant bonding scale (MIBS) (Taylor et al., 2005). Edinburgh Postpartum Depressive Scale (EPDS). Maternal adult attachment style Infant behavioural characteristics Interviewed by a paediatric psychiatrist.	13% rates of impaired mother-infant bonding. MIBS ≥ 2 satisfactorily detected difficulties in mother-child bonding. MIBS score was influenced by the infant's behavioural characteristics.	Weak Strengths: Adequate sample size Interview with a psychiatrist to confirm impaired bonding. Limitations: Response rate not reported Ethnicity, maternal education were not reported Psychiatric history and psychological vulnerability not explained properly.
2	Edhborg et al. (2005) Sweden	Prospective cohort Study. N=106 (couples)	Data collection: 2 time-points One week and two months post-delivery. Measures: 4 self-rating questionnaire. Demographic and obstetric	9% of impaired mother – infant bonding was reported at 1 week and 1% at 2 months postnatal. Previous depression in	Weak Strengths: Adequate sample size Adequate follow-up

Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
	Setting: Hospital Maternity ward	characteristics. The Blues Questionnaire (Kennerley and Gath, 1989) Postpartum Bonding Questionnaire (PBQ) (Brockington 2001). Edinburgh Postpartum Depressive Scale (EPDS). The Infant Characteristic Questionnaire (ICQ;) (Bates et al., 1979)	life was related to both the EPDS and the PBQ at two months in the mothers. Similarities between mothers and fathers were found in symptoms of blues, impaired bonding at one and two months. EPDS \geq 10 was related to impaired mother-infant bonding at two months. Fussy-difficult infant.	Limitations: High dropout rate limited the generalisability of the study. 429 couples agreed to take part but only 106 (25%) completed the study Previous depression reported by participants was not clearly explained, i.e. whether mild, diagnosed or treated Lower EPDS threshold \geq 10 used instead of recommended \geq 12/13.
3 Edhborg et al. (2011) Bangladesh	community-based cohort study carried out in rural Bangladesh N= 672 Setting: Participants homes	Data collection: 2 time-points 3 rd trimester of pregnancy and 2-3 months post birth. Measures: 5 questionnaire administered by the researcher. Demographic information. Edinburgh Postnatal Depression Scale (EPDS; Cox et al. 1987). State Anxiety Inventory (STAI-S; Spielberger 1983).	11% of the mothers reported impaired mother-infant bonding. Depressive symptoms (EPDS \geq 10) and giving birth to a girl were negatively associated to mother-infant bonding.	Moderate Strengths: Large sample size Data analysis clearly described. Limitations: Lower EPDS threshold \geq 10 Study conducted in a low income country may not be relevant to

	Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
			Postpartum Bonding Questionnaire (PBQ; Brockington et al. 2001). Prenatal Attachment Inventory (PAI); (Muller, 1993). Parental Bonding Instrument (PBI); (Parker et al., 1979).	Maternal anxiety symptoms and high bonding to the fetus during pregnancy were positively associated to mother- infant bonding 2–3 months postpartum.	high income countries Possibility of reporting bias as questionnaire administered by staff, so participants may have given socially desirable answers.
4	Figueiredo et al. (2007) Portugal	Prospective cohort Study. N= 456 (315 mothers and 141 fathers) Setting:	First 2 days after delivery. Measures: 2 self-rating questionnaire. Bonding Scale (validated and extended Portuguese version of the 'New Mother-to-Infant Bonding Scale Taylor et al; 2005). Edinburgh Postnatal Depression Scale (Portuguese version).	4% of mothers and 2% of fathers reported impaired mother-infant bonding. No statistical significant differences between mother-to-infant and father-to-infant bonding.	Weak See below as same study but maternal data reported separately two years later.
5	Figueiredo et al. (2009) Portugal	Cross sectional study N=315 Setting: Postnatal ward of a maternity	First 2 days after delivery. Measures: Questionnaire administered by researcher. Participants were interviewed to obtain social, demographic and background data, as well as	EPDS≥13. Lower educational level. Unemployed and single. Giving birth to a female.	Weak Strengths: Adequate sample size EPDS≥13 Limitations:

	Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
		hospital	information about childbirth and the infant; which includes (Previous Life Events, type of delivery, pain at childbirth, support from partner, infant characteristics and early contact with the new-born. Bonding Scale (validated and extended Portuguese version of the 'New Mother-to-Infant Bonding Scale Taylor et al., 2005). Edinburgh Postnatal Depression Scale (Portuguese version).	infant. Mother-infant bonding was not related to event related to childbirth i.e. (neither type of delivery, pain relief in labour, support from partner during delivery nor early contact with the infant).	Possible selection bias, as the author recruited 99% Caucasian which limited the generalisability of the study The author claimed a 98% compliance rate but did not give details of how participants were approached and how many provided complete data Questionnaire was administered by the researcher hence participants could have given social desirable answers Validity of the translated version was only reported by the same research team.
6	Figueiredo and Costa (2009) Portugal	Prospective cohort Study. N=91 Setting: Obstetrics Outpatient	Data collection : 2 time-points 21 -28 weeks gestation and three months postnatal. Measures: Socio-demographic information. Self-rating questionnaires. 24-hour urine sample.	Maternal antenatal anxiety predicted a worse emotional involvement with the infant after birth. Maternal state anxiety and depression did not	Weak Similar limitations as in the above study by same research group Period of recruitment was not stated unsure which study was first

	Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
		Hospital Unit	<p>State-Trait Anxiety Inventory (STAI, Spielberg et al. 1983).</p> <p>Edinburgh Postnatal Depression Scale (EPDS, Cox et al. 1987).</p> <p>Bonding Scale (a validated and extended Portuguese version of the 'New Mother-to-Infant Bonding Scale' (Taylor et al. 2005).</p>	<p>predict cortisol levels of the mother.</p> <p>Cortisol levels did not predict the mother's emotional involvement with the child either during pregnancy or postnatal period.</p>	<p>Antenatal anxiety was measured with MIBS which has not been validated to use in pregnancy.</p> <p>The authors examined maternal emotional involvement with the infant with MIBS. It was unclear if this is the same as impaired mother to infant bonding.</p>
7	Gunning et al. (2011) United Kingdom	Cross sectional study N=64 Setting: Community	<p>4 months postnatal.</p> <p>Questionnaire administered by researcher and videotaped mother-infant interaction</p> <p>Measures: 4 self-rating questionnaire. Demographic information. Adult attachment style ((The relationship questionnaire(RQ) (Bartholomew and Horowitz, 1991) Emotional Intelligence Test (Palmer and Stough, 2001). Postpartum Bonding Questionnaire</p>	<p>Greater attachment anxiety was associated with higher levels of impaired bonding.</p>	<p>Weak</p> <p>Limitations: Small sample size Selection bias: participants were identified using a postcode data from the Scottish Index of Multiple Deprivation (SIMD) (Scottish Executives, 2006) , thereby recruited only vulnerable groups, i.e. only women with low incomes or socially deprived limiting generalisability of the study.</p>

	Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
			(PBQ; Brockington et al. 2001). Maternal play behaviour (Atypical Maternal Behaviour Instrument for Assessment and Classification (Lyons-Ruth et al., 1999).		
8	Kokubu et al. (2012) Japan	Prospective cohort Study. N= 99 Setting: Antenatal clinic of a maternity hospital	Data collection : 3 time- points 33-35 weeks gestation. 5 days and 1 months postnatal Measures: 5 self-rating questionnaire. The Hospital Anxiety and Depression Scale (HADS); (Zigmond and Snaith, 1983). Negative attitudes towards pregnancy (developed for the study) Maternity Blues Questionnaire (MBQ); (Stein, 1980). Edinburgh Postnatal Depression Scale (EPDS; Cox et al. 1987). Japanese translated version (Mother-Infant Bonding Questionnaire (Taylor et al., 2005).	Maternal negative attitude towards pregnancy was correlated with bonding failure (MIBQ) scores at both day 5 and month 1 after childbirth. No correlation between late pregnancy anxiety and bonding failure or between late pregnancy depression and during postnatal period. Impaired bonding at day 5 was correlated with depression 1 month postnatal	Weak Strengths: Adequate sample size Limitations: Author did not control for socio- demographic factors such as maternal education and marital status High response rate (96%) but the author did not report how participants were approached and recruited. Validity and reliability of instrument used was not reported

	Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
9	Moehler et al. (2006) Germany	Prospective cohort Study. N=101 Setting: four local obstetric units	Data collection : 4 time-points two weeks, six weeks, four months and fourteen months postpartum. Measures: 3 self-rating questionnaire. Maternal psychopathology was measured via the revised Symptom Checklist (Derogatis et al., 1973), The Edinburgh Postnatal Depression Scale (EPDS) Cox et al, 1987). Postpartum Bonding Questionnaire (Brockington et al., 2001.)	Depressive symptoms in the early postnatal period influence maternal bonding almost a year later. The impact of maternal depressive symptoms on bonding was most pronounced at six weeks postnatal Mother-infant bonding was moderately stable across the four time- points	Data analysis was not clearly described. Strong Strengths: Adequate sample size Multiple sites Power calculation reported Response rate reported (87% response rate) Validity and reliability of the instrument reported Long follow-up period (more than a year) Limitations Pregnancy related variables were not mentioned.

	Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
10	Müller et al. (2013) Germany	Prospective cohort Study N=66	<p>Recruited via advertisements in Hospitals, medical practices, and via the internet.</p> <p>Data collection: 2 time-points 36 weeks gestation and 5 weeks postnatal.</p> <p>Measures: 4 self-rating questionnaire Perseverative Thinking Questionnaire (PTQ) (Ehring et al., 2011). Beck Depression Inventory-II (BDI-II; (Beck et al., 1996) German version Postpartum Bonding Questionnaire (PBQ; Brockington et al.2001; German Version: (Reck et al., 2006).</p> <p>Attachment Scale of the Parenting Stress Index, German version (PSI; (Loyd and Abidin, 1985).</p>	<p>Antenatal ruminative thinking (e.g. repetitive, difficulty to disengage from, unproductive and capturing mental capacity)</p>	<p>Weak</p> <p>Limitations Small sample size.</p> <p>Selection bias, as participants were recruited through advertisements in hospitals, medical practices and on the internet. It may not be representative of the population as women who responded might be interested in the study. Women who did not respond may have provided a different outcome</p>

	Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
11	Muzik et al. (2013) USA	Prospective cohort Study N=150 Setting:	Data collection : 3 time-points Six weeks, four and six months postnatal. Measures: 5 self-rating questionnaire. Demographic questionnaire (describing yearly household income, maternal race, age, years of education, and marital relationship). Postpartum Bonding Questionnaire (PBQ; Brockington et al.2001. Maternal childhood trauma CTQ (Bernstein et al., 2003). Maternal PTSD : National Women's Study NWS; (Resnick et al., 1993). Postpartum Depression Screening Scale (PPDS;(Beck and Gable, 2000) Observed maternal behaviours (Videotaped during a 10-min in- home, free-play was coded with the MACY Infant-Parent Coding System (Earls, 2010).	Postpartum depression and Posttraumatic stress disorder PTSD were associated with impaired mother-infant bonding.	Moderate Strength: Adequate sample size Adequate follow-up Data analysis was clearly described. 37% missing data however attrition analysis describing patterns of missing data was reported. Limitations: Power calculation was not reported. Sample bias; Over represented sample of mothers with a history of child abuse may have resulted in over reporting of the outcome of interest.

	Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
12	O'Higgins et al. (2013) United Kingdom	Prospective cohort/ intervention Study N=79 (n = 50 study group n = 29 control group) Setting: Postnatal ward	Data collection : 4 time-points 4 , 9, 16 weeks and 1 year postnatal Measures: 2 self-rating questionnaire and baby massage classes. Socio-demographic information EPDS (Cox et al.1987). The MIBQ (Taylor et al.2005) Baby massage classes/ support groups.	There were no differences in bonding scores at any time point between the women who attended baby massage classes and the women who attended a support group Early impaired bonding at 1-4 weeks postnatal was the main predictor of impaired bonding at 1 year.	Moderate Strengths': Moderate sample size Comparing groups at baseline and follow up three times Attrition was reported Limitations: Lack of generalisability of the study Study excluded women with housing or social problems Low response rate of (31%). Over represented sample of women with postnatal depression Author claimed that control groups were randomly selected but did not clarify how it was done.

	Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
13	Reck et al. (2006) Germany	Longitudinal prospective study N=862 Setting: In- patients of delivery units	Data collection: 2 weeks postnatal Measures: 2 self-rating questionnaire and structured interview. The Edinburgh Postnatal Depression Scale (EPDS; Cox et al,1987; German translation by Bergant et al, 1998) The Structured Clinical Interview for DSM-IV, Axis I(SCID-I; (Wittchen et al., 1997). The Postpartum Bonding Questionnaire (Brockington et al.2001).	7% rate of mothers with bonding impairment two weeks postpartum Low level of education and postnatal depression had a significant association with impaired mother-infant bonding	Moderate Strengths: Large sample size Validity and reliability of instrument reported Data analysis clearly explained. Limitations: Recruitment strategy and response rate not described Only German speaking women were recruited limiting the generalisability of the study Possible confounders not mentioned e.g. information about childbirth not mentioned. Author claimed that study was a longitudinal prospective study but only data at 2 weeks postnatal was reported no indication as when participants were recruited.

	Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
14	Taylor et al. (2005) United Kingdom	Prospective cohort study N=144 Setting: postnatal ward	Data collection: 2 time-points. Day 3 and twelve weeks postnatal. Measures: 3 self-rating questionnaire. Kennerley Blues Scale (Kennerley and Gath, 1989). Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987). The Highs Scale, for the detection of mild sub clinical hypomania (Glover et al., 1994).	9% rate of impaired mother-infant bonding Depressive symptoms (EPDS \geq 13) at 3 days and 12 weeks postnatal was strongly correlated with impaired mother-infant bonding at each time- points	Moderate Strengths: Adequate sample size Data analysis clearly described. Validity of the instrument reported Limitations: Confounding factors such as socio-demographic variables were not reported in the analysis Bonding at first week was retrospective which could result in possible recall bias

	Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
15	van Bussel et al. (2010b) Belgium	Longitudinal prospective study N=263 Setting: Antenatal clinic	Data collection at 5 time points. 8–15, 20–26, and 30–36 gestation. 8–12 and 20–25 weeks postpartum. Measures: 11 self-rating questionnaire Attachment Scale (Condon and Corkindale, 1998). Postpartum Bonding Questionnaire (Brockington et al. 2001). Mother-to-Infant Bonding Scale (Taylor et al. 2005). Participants' tendency to respond in a socially desirable manner Marlowe-Crowne Social Desirability Scale (MCSDS-10: Crowne and Marlowe 1960; (Strahan and Gerbasi, 1972). Dutch version of the Parental Bonding Inventory (PBI;(Parker et al., 1979)	Multiparous women and highly educated women reported lower feelings of bonding with their newborn infants. Women with more antenatal feelings of closeness and tenderness towards their fetuses reported better mother-infant bonding postnatally. Women with more or stronger depressive or anxiety symptoms reported lower feelings of bonding with their infants	Moderate Strengths: Adequate sample size Adequate follow-up (5 times) Validity and reliability of instrument reported Data analysis and response rate clearly described Limitations: The author reported a 93% response rate, but it was unclear how participants were recruited as inclusion and exclusion criteria were not mentioned. Power calculation was not reported. Multiple measures were used (11) but the author did not report any post hoc test e.g. (Bonferroni correction) to counteract the

Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
		<p>Participant's attachment style with Dutch version of the Relationship Questionnaire (RQ: (Bartholomew and Horowitz, 1991).</p> <p>Maternal Antenatal Attachment Scale (MAAS: Condon 1993).</p> <p>Participant's antenatal orientation on motherhood: (van Bussel et al., 2009).</p> <p>Edinburgh Postnatal Depression Scale (EPDS: Cox et al. 1987)</p> <p>Anxiety subscale of the Dutch version of the Hospital Anxiety and Depression Scale (HADS-A: (Zigmond and Snaith, 1983).</p> <p>Maternal Separation Anxiety Scale (MSAS: (Hock et al., 1989).</p>		<p>problem of multiple measures creating a possibility of type 1 error.</p>
<p>16 Wittkowski et al. (2007)</p> <p>United Kingdom</p>	<p>Cross sectional study N=96 Postnatal ward</p>	<p>Between day 2 - 4 Measures: 3 Self-report questionnaire:</p> <p>The Postpartum Bonding Questionnaire (Brockington et al., 2001)</p>	<p>Association with impaired bonding was not state. But study findings indicated that PBQ & MIBS demonstrated acceptable reliability and reasonable validity</p>	<p>Weak</p> <p>Strength: Adequate sample size</p> <p>Limitations: Lack of representation and</p>

Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
		Mother-to-Infant Bonding Scale (Taylor et al., 2005) The Kennerley Blues Scale (Kennerley and Gath, 1989)	The bonding scores improved in the early postpartum period.	<p>generalisability of the findings as the study excluded</p> <p>Women who were separated from their infant more than four hours after delivery.</p> <p>Excluded women may have provided different outcomes.</p> <p>Data was collected retrospectively after birth and on days 2-4 postnatal. The author claimed that the bonding scores improve in the early postpartum period but their follow-up was too short to find any difference in maternal feelings towards the infant as the data was compared between day1 and day 2-4 postnatal).</p>

	Author, year and country	Study design and sample	Data collection and instruments	Key findings related to impaired mother-infant bonding	Quality of study
17	Yoshida et al. (2012) Japan	Longitudinal prospective study N=554 Setting: Postnatal Ward	Data collection: 3 time-points. Day5. 1 month. 4 months postnatal. Measures: 2 self-report questionnaire. Socio-demographic information. Mother to Infant Bonding Scale MIBS (2005) (Japanese translated version). Depressive symptoms (EPDS).	Depressive symptoms (EPDS=>9)	Moderate Strengths: Large sample size 3 times follow-up Limitations: Measurement bias. The questionnaire used has not been validated by other authors. Study used EPDS score of 9 and above which was different from the recommended 13 and above.

Abbreviations: EPDS, Edinburg Postnatal Depression scale; DSM-1V, Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; SCID-I, Structured Clinical Interview for DSM-IV Axis I Disorders; STAI-S, State-Trait Anxiety Inventory-Scale; PAI, Prenatal Attachment; PB1, Parental Bonding Instrument; PBQ, Postnatal Bonding Questionnaire; PSI, Parenting Stress Index; PTSD, Posttraumatic Stress Disorder; MCSDS, Marlowe-Crown Social Desirability Scale; MIBS, Mother Infant Bonding Scale; PTO, Perseverative Thinking Questionnaire.

2.3 Exposure variables

The exposure variables in the selected studies included maternal emotional wellbeing, assessed either by maternal depression, anxiety or transient psychological problems ('maternity blues'). Maternal depression was assessed using the Beck Depression Inventory Questionnaire (Müller et al., 2013) or the Hospital Anxiety and Depression Scale (Kokubu et al., 2012; Van Bussell et al., 2010).

Seven studies of the 11 studies screened for maternal depressive symptoms using the EPDS (Cox et al., 1987), although the cut-off score used to identify women at risk of depression varied between studies. For example, Edhborg et al. (2005) used a cut off of ≥ 10 for a Swedish population and in their subsequent study of a Bangladeshi population (Edhborg et al., 2011), whereas a lower cut off of ≥ 9 was chosen by Yoshida et al. (2012). In addition, maternal anxiety (Edhborg et al., 2011) and maternal blues (Edhborg et al., 2005; Wittkowski et al., 2007) were assessed as part of maternal emotional wellbeing. Three of the studies assessed women's negative attitude towards pregnancy (Kokubu et al., 2012) and maternal antenatal attachment to their unborn baby (Edhborg et al., 2011; van Bussel et al., 2010) as potential predictors of impaired mother-to-infant bonding.

Other exposure variables included infant behavioural characteristics at two days postpartum, i.e. alertness, excitability, and capacity to self-quiet (Bienfait et al., 2011); infant characteristics at 2 months (infant temperamental traits) (Edhborg et al., 2005); measurement of maternal own bonding to her care giver, (Parental Bonding Instrument, PBI (Parker et al., 1979) (Edhborg et al., 2011; Gunning et al., 2011; van Bussell et al., 2010). In general, the exposure variables observed in the included studies varied depended on the primary aim of the study. Most authors relied on the assessment of maternal emotional wellbeing as a predictor of impaired mother infant bonding. Measurement of other factors which could have been possible contributing factors of impaired bonding, such as difficulty at childbirth, lack of social support and previous life events was inconsistent.

2.4 Findings

The estimated rate of impaired infant - bonding, as measured by self-rated scales in selected studies, ranged from 4–13% in non-clinical perinatal population. Confidence intervals and odds ratios for prevalence were only presented in one study (Reck et al., 2006). This variation may be explained by the different instruments used to measure mother-to-infant bonding and the time it was measured. Generally, the earlier the measure, the higher the rate of impaired mother-infant bonding found.

The main finding was the association between maternal postnatal depressive symptoms as assessed by EPDS and impaired mother-to-infant bonding measured by either the PBQ Brockington et al. (2001), (Edhborg et al., 2005, 2011; Moehler et al., 2006; Muzik et al., 2013; van Bussel et al., 2010) or Taylor et al.'s (2005) Mother to Infant Bonding Scale (Bienfait et al., 2011; Figueiredo et al., 2009; Taylor et al., 2005). Nine of the 17 studies reviewed reported this association. However, the threshold score for predicting postpartum depression with the EPDS varied from 9 (Yoshida et al., 2012) to 13 (Figueiredo et al., 2009; Taylor et al., 2005). Moreover, depressive symptoms in the early postpartum period were more likely to be associated with impaired bonding than depressive symptoms at one year post-partum (Moehler et al., 2006; O'Higgins et al., 2013).

Other factors identified as associated with impaired maternal bonding, included giving birth to a female child (Edhborg et al., 2011; Figueiredo et al., 2009), maternal negative attitude towards pregnancy (Kokubu et al., 2012), maternal bonding at first week of birth (Edhborg et al., 2005; O'Higgins et al., 2013), and

infant temperament (Edhborg et al., 2005). Low maternal education was also reported as a factor associated with impaired maternal bonding (Reck et al., 2006; Figueiredo et al., 2009). In contrast van Bussell et al. (2010) reported a high maternal level of education as a factor that was associated with maternal impaired bonding in their study.

2.5 Discussion

The aims of this review were to examine the prevalence and factors associated with impaired mother to infant bonding in women with no known diagnosis of mental health problems during pregnancy. The estimated prevalence of poor mother to infant bonding found in the population groups in selected studies varied, ranging from 1–12%. However, studies were more likely to report high prevalence rate of impaired mother to infant bonding if conducted in the first week post birth. This may not be a true reflection of impaired bonding as most prior research that assessed impaired bonding at different time points reported a general improvement in bonding score (Edhborg et al., 2005; Edhborg et al., 2011; Kokubu et al., 2012; Moehler et al., 2006; Muzik et al., 2013; O'Higgins et al., 2013; Taylor et al., 2005; van Bussell et al., 2010; Yoshida et al., 2012), which supports earlier observations by (Robson and Kumar, 1980). The possible explanation for the improvement in impaired bonding is that early impaired bonding reported in these studies could be as a result of circumstances surrounding the birth and need not imply that the woman actually have impaired bonding. Therefore, studies conducted later than six weeks post birth would be more appropriate in determining the prevalence of impaired bonding. The principle findings of the reviewed studies on the factors

associated with impaired mother-infant bonding consistently revealed that impaired maternal bonding was related to maternal emotional state, and in particular, postnatal depression. However, most studies were of poor quality which prevented a greater understanding of associated factors. Most did not account for or did not adequately address other factors relevant to mother-infant bonding. For instance, the majority of studies did not include or mention social support, infant characteristics, demographic information (ethnicity, maternal education, and/or socioeconomic status), pregnancy variables or birth experience.

Despite increasing evidence that antenatal depression and anxiety are the main predictors of postnatal depression (Leigh and Milgrom, 2008, Piacentini et al., 2009, Banti et al., 2011, Coelho et al., 2011, Siu et al., 2012, Youn and Jeong, 2013), only two studies (Figueiredo and Costa, 2009; Kokubu et al., 2012) included in this review examined the effect of antenatal emotional state on mother-infant bonding, association between postnatal depression and impaired mother-infant bonding identified could have originated during pregnancy.

2.6 Limitations

The search strategy excluded studies that measured impaired bonding with a validated questionnaires, which mainly included two measures the PBQ and MIBS, and studies which did not specifically measuring mother - infant bonding. As a result, important work may have been overlooked, as some authors consistently used other terms, such as maternal infant attachment, mother to

infant relationship and mother infant bonding interchangeably (Bienfait et al., 2011).

There was also the possibility of publication bias as the current review excluded studies not published in English (Egger et al., 1997). In addition, impaired mother to infant bonding detection bias may have occurred due to the wide variations of infant age at the time of assessment (<3 days to one year). Finally, the review included only one study from a low income country, which requires careful interpretation as the factors that impact on impaired mother-to-infant bonding may be different for low and high income countries.

The findings highlighted the need for an appropriately designed study to enhance the understanding of antenatal factors associated with impaired mother to infant bonding including antenatal depression, anxiety, life events and antenatal fetal bonding. The identification of women at risk of impaired maternal bonding during pregnancy could lead to early interventions to enhance mother to infant relationships which could subsequently facilitate good parenting practices. The research undertaken for this thesis had the aim of overcoming methodological limitations of previous studies.

CHAPTER 3 METHODS

3.1 Introduction

This chapter will describe the research method and tools used to meet the research aims and objectives. The chapter will justify the choice of method and selection of study measures based on the literature reviewed and presented in Chapter 2. As the research design, sampling procedures, setting, participants, measures, data collection procedures, data analysis strategy (linked to objectives), ethical approval and ethical considerations are detailed in a systematic, comprehensive, explicit and reproducible manner, transparency of study findings are optimised.

3.2 Study aims and objectives

To reiterate, the primary aim of this study was to identify factors in pregnancy that could predict early mother-infant bonding problems at six weeks postnatal, focusing primarily on the maternal emotional state during pregnancy, using self-report questionnaires. A secondary aim was to assess if a high risk pregnancy could affect mother-to-infant bonding. To address these aims, the following objectives, research questions, and hypotheses were formulated:

The specific objectives were to:

1. To assess whether maternal self-reported measures of anxiety, depression and other psychosocial measures in late pregnancy would predict poor mother-infant bonding at 6 weeks post birth.
2. To examine the relationship between maternal postnatal psychometric measures and mother-infant bonding scale at 6 weeks postnatal.

3. To assess whether having a high risk pregnancy would affect mother-infant bonding postnatal.

3.2.1 Research questions

1. Does depression or other psychological problems in late pregnancy predict poor mother-to infant bonding at six weeks postnatal?
2. Do psychometric measures of postnatal anxiety or depression correlate with the Mother to Infant Bonding Scale?
3. Does having a high obstetric risk pregnancy affect mother-infant bonding?

3.2.2 Hypotheses

3.2.2.1 Primary hypothesis

Maternal anxiety, stress, depression and poor fetal bonding during late pregnancy are related to early mother-infant bonding problems 6 weeks postnatal.

3.2.2.2 Secondary hypothesis

- Having a high risk pregnancy is associated with poorer mother-infant bonding.
- A high level of maternal postnatal anxiety and depressive symptoms is associated with impaired mother-infant bonding at 6 weeks postnatal.

3.3 Ethics approval

Ethics approval was obtained from Charing Cross Hospital Ethics Committee (Appendix 4). The study was also conducted in accordance with the Research Governance Framework for Health and Social Care and Good Clinical Practice (GCP) (DoH, 2005). It was approved by Imperial College Healthcare NHS Trust Research Governance (see appendix 5).

3.4 Study design

A longitudinal prospective cohort study was undertaken, with self-report questionnaires, to investigate antenatal predictors of early mother-infant bonding problem at six weeks postnatal. Data were collected from each participant at two time points: Time 1 (late pregnancy), and Time 2 (six weeks postpartum). Data were collected over a four year period (2008-2012).

As the study was concerned with identifying associations and trends over time in a sample who shared the same event (i.e., singleton birth cohort), a large scale longitudinal cohort type study was appropriate. To test study hypotheses, a research approach was required that would enable causal predictions of the role of mood (depression, anxiety, stress), maternal personality disorder, maternal-fetal bonding, and high obstetric risk factors during pregnancy, on maternal-infant bonding outcomes postnatally. The independent variables included maternal perinatal anxiety, maternal state-trait anxiety, maternal antenatal and postnatal stress, stressful life events, maternal antenatal and postnatal depression, maternal personality disorder, and maternal-fetal bonding. The dependent variable (outcome measure) was the mother-to-infant bonding

score, measured using a binary variable with two categories: (1) good bonding (score <2), and (2) poor bonding (score ≥2). Potential confounding variables measured included maternal age, marital status, self-assigned ethnicity, and maternal socioeconomic status, country of birth, parity, smoking status, and alcohol intake in pregnancy. The mediator variables measured (identified in the literature as associated with mother-infant bonding) included: social support; pregnancy, labour and birth outcomes; neonatal outcomes, and breastfeeding.

3.4.1 Rationale for study design

Cohort studies are considered the ‘gold standard’ for risk-factor analysis as they allow for the collection of unbiased risk factor information (Zondervan et al., 2002) and their design may be prospective or retrospective.

A prospective cohort design can be used to determine the natural history, incidence and causes of an outcome. It is particularly important, because it can provide evidence of a causal link between two variables as it measures potential causes before the outcome has occurred, avoiding the question as to which variable is the cause and which is the effect (Mann, 2003). Moreover, a prospective cohort study allows for calculation of the effects of each variable on the likelihood of developing the outcome of interest (Mann, 2012). However, there are some limitations which should be considered. Cohort studies are time consuming and expensive and loss to follow-up (drop-out) may introduce attrition bias. This means that there is the potential that the sample studied may not be representative of the population (Mann, 2003, Yang et al., 2010, Besen and Gan, 2014).

A prospective cohort design was deemed the most appropriate for this study for several reasons: First, relevant retrospective data on the cohort were not available, and as the study aim was to determine risk factors for impaired mother-infant bonding, it was important that all relevant data were collated from the outset before the participants developed the problem. Second, a prospective design enabled potential risk factors in pregnancy to be measured (i.e. antenatal psychological and biological status) to be collected before the outcome of interest (i.e. poor mother-infant bonding), in the same population of women. Third, collecting data prospectively allowed the researcher to demonstrate if antenatal predictors of interest were associated with the postnatal outcome, and infer causation (Katz, 2006; Mann, 2003).

Other observational designs were considered, while cross-sectional designs are helpful in identifying potential association between different variables; they would not allow the examination of a cause and effect relationship between the psychosocial or emotional factors and mother-infant bonding. A cohort design would minimise the likelihood of reverse causality, in which the outcome causes the risk factor rather than vice versa (Katz, 2006, Song and Chung, 2010).

A case-control design was also considered, but was deemed inappropriate for this study because it would require use of a reference group (participants without the bonding disorder) and a comparison group (participants with the bonding disorder), with all the comparisons being made retrospectively (Zondervan et al., 2002, Gerrish and Lacey, 2010). As screening for poor

mother-infant bonding is not currently part of routine postnatal care, incidences would not be available within the population studied.

3.5 Study measures

Two types of measures were selected for use in this study: (1) psychological measures (in the form of self-rating questionnaires), and (2) biological measures (in the form of saliva samples from the women and explored in 'nested' pilot study, discussed in the next chapter). Five standardised self-report questionnaires were used to measure the independent variables namely maternal anxiety, stress, depression, personality disorder, and fetal bonding. Maternal socio-demographic and obstetric variables were measured using a demographic and clinical characteristics questionnaire (e.g. marital status, education, employment, pregnancy, labour and neonatal outcome). The dependent variable, impaired mother-infant bonding score, was measured using the Mother Infant Bonding Scale (Taylor et al., 2005). Details of each measure used are reported below.

3.5.1 Independent variable measures

3.5.1.1 Assessment of maternal perinatal anxiety

Approaches to measure perinatal anxiety has varied across different studies. Some previous studies have assessed maternal anxiety using general anxiety measures (i.e. measures of anxiety developed for use in the general population but used with perinatal women) which includes The Hospital Anxiety and

Depression Scale (Zigmond and Snaith, 1983); The State-Trait Anxiety Inventory (STAI) (Spielberger et al., 1983) and the Beck Anxiety Inventory (Steer and Beck, 1997). A number of pregnancy specific anxiety measures (measures developed specifically to screen for aspects of perinatal anxiety with questions not relevant to the general population) have been developed, including the Pregnancy Anxiety Scale (PAS), (Levin, 1991); Pregnancy-Related Anxiety Questionnaire-Revised (PRAQ), (Van den Bergh, 1990) or the Perinatal Anxiety Screening Scale (PASS), (Somerville et al., 2014). However, the Spielberger State-Trait Anxiety Inventory (STAI) was chosen in the current study as this was the most commonly used measure of anxiety in previous perinatal studies (Meades and Ayers, 2011), meaning that potential comparison could be made with the results of the current study.

3.5.1.1.1 Maternal State-Trait Anxiety Inventory

The Spielberger State-Trait Anxiety Inventory (STAI), (Spielberger et al., 1983), (appendix 29) is a self-complete questionnaire consists of two parts, each with 20 items, aimed at assessing feelings of tension and anxiety. It clearly differentiates between the temporary condition of “state anxiety” (an individual’s current feelings), and the more general and long-standing quality of “trait anxiety” (how they generally feel) (Bieling et al., 1998). The measure is rated on a four point Likert scale (1-4), with the total score ranging between 20 and 80 and higher scores indicating high state or trait anxiety. It has been shown to have high reliability and validity (Bieling et al., 1998, Bergman et al., 2007, Gunning et al., 2010, Dennis and Dowswell, 2013). It has been used widely in pregnancy (Hart and McMahon, 2006, Austin et al., 2007, Grant et al., 2008,

Meades and Ayers, 2011) and postnatal studies (Barnett and Parker, 1986, Grant et al., 2008, Dennis and Dowswell, 2013).

The results of the STAI can be used to support a clinical diagnosis to differentiate anxiety from depression in psychological and health research (Mindgarden, 2008). In the current study, it was used to differentiate whether maternal antenatal anxiety rather than depression would predict poor mother-to-infant bonding. That is, in the first part of the questionnaire, the women were asked to report how they felt at present (within the last 24 hours) and in the second part how they generally felt. A total score of 40 or more in either subscale was the cut-off used, as this is considered indicative of high anxiety in other studies (Barnett and Parker, 1985, Hart and McMahon, 2006, Dennis et al., 2013).

Other researchers have used a shortened version of the State & Trait anxiety inventory or the State dimension of STAI but not the Trait dimension to assess maternal anxiety in perinatal research, (Roesch et al., 2004, Bayrampour et al., 2014), although, it has been reported that the shortened version of STAI may be problematic in clinical practice (Kruyen et al., 2013).

The current study used both the State & Trait anxiety inventory to differentiate between the woman's anxious state at the time of assessment from her predisposition or more permanent characteristic of her personality (Adedinsewo et al., 2014, Dubber et al., 2014). In addition, both State and Trait anxiety scales demonstrated a reasonable estimation of antenatal clinical state when tested against the Mini-plus diagnostic interview (DSM-IV) during pregnancy (Grant et al., 2008).

3.5.1.2 Assessment of maternal antenatal and postnatal stress

A range of instruments have been used as indicators of maternal stress in previous research, including individual perception of stress or reaction to an event (Nast et al., 2013). These measures have included measures of life events (Barnett et al., 1983); daily hassle (Cohen et al., 1983, Brantley et al., 1987) and anxiety (Spielberger, 1983).

Life events are the most common type of stressor studied in prenatal stress research, however, the instruments used have varied, with some researchers (Sjostrom et al., 1999, Bergman et al., 2007, Phillips et al., 2010) using either the modified or original version of the Inventory of Ranked Life Events for Primiparous and Multiparous women (Barnett et al., 1983), whilst others, (Dole et al., 2003, Wurmser et al., 2006, Pluess et al., 2010), have used the Life Experience Survey (Sarason et al., 1978) or the Prenatal Life Events Scale (Lobel et al., 1992), as used in (Saunders et al., 2006, Glynn et al., 2008) studies.

Maternal antenatal and postnatal stress were measured in the current study using the Stressful Life Events Scale (Bergman et al., 2007), at 36 weeks gestation and six weeks postnatal, (appendix 31). This questionnaire consists of 26-item measures of exposure to stressful life events and was adapted from work completed by Barnett et al. (1983). The SLES is a list of normative stressors; the original version was developed specifically for obstetric groups. Items selected from the original inventory were those identified as being relevant to both antenatal and postnatal populations (Bergman et al., 2007).

The questionnaire has not been validated but has been used in other studies (King et al., 2010, Giesbrecht et al., 2012).

The women recruited to the current study were asked to indicate if the event occurred and if so, whether it “affected me a little” or “affected me a lot”. They also reported whether the event occurred prenatally or postnatally when asked at the six week postnatal follow-up. The scoring of the questionnaire resulted in two readings: an objective number and the perceived impact of the events experienced. Items were scored on a 0-2 scale: non-occurrence of the event (0); the event “affected me a little” (1) or it “affected me a lot” (2). The range of the total scores for the objective number of events experienced was 0-26, and consequently for the perceived impact of stressors was 0-52. The total of the objective number was added to the perceived effect for each woman to obtain an overall estimate of maternal stress in pregnancy.

3.5.1.3 Assessment of maternal antenatal and postnatal depression

A number of self-report measures have been used in perinatal populations to assess an individual’s risk of depression, including the General Health Questionnaire (Goldberg and Williams, 1988), the Beck Depression Inventory Scale (Beck et al., 1996), The Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983) and the Whooley questions (Whooley et al., 1997) recommended for routine identification of women who may be at risk of developing depression in the NHS in England and Wales (NICE, 2007). The EPDS (Cox et al., 1987) was selected for this study, because it is the most

widely used questionnaire in perinatal research and has been robustly validated (Gibson et al., 2009, Milgrom and Gemmill, 2014).

The EPDS (COX et al., 1987), (appendix 30) is a ten-item scale, which is self-administered and requires about five minutes to complete. It was developed to assist health care professionals to detect women with a high probability of suffering from postnatal depression, although it has now been validated for use during pregnancy (Cox and Holden, 2003). The total EPDS score ranges from 0-30, a score of 13 or more being indicative of major depressive symptoms (Cox et al., 1987). The sensitivity of the EPDS was originally validated against a diagnosis of depression using major and minor research diagnostic criteria (RDC) (Spitzer et al., 1978) by Cox et al. (1987). They found that sensitivity (the proportion of true positives) was 86% and the proportion of true negatives was 78%, whereas the positive predictive value (the proportion of women above the threshold on the EPDS who met the RDC for depression) was 73% (Cox et al., 1987).

For this study, women were asked to complete the scale at 36 weeks gestation and six weeks postnatal. In line with guidance from the developers of the EPDS, the women were asked to consider the 10 item questionnaire relating to symptoms of depression with respect to their feelings during the previous seven days and to choose one of four possible answers which best reflected these. Responses were rated on a four point scale (0, 1, 2 and 3) and the scores were aggregated to give a final score which could range from 0 to 30. A total score of 13 and above was used as a cut-off score for possible depression as it is the

recommended value indicating possible depression (Cox et al., 1987, Matthey et al., 2006).

3.5.1.4 Assessment of maternal-fetal bonding (antenatal attachment)

Several studies have supported the antenatal root of postnatal bonding (Muller, 1996, Condon and Corkindale, 1997, Siddiqui and Hägglöf, 2000, Damato, 2004, van Bussel et al., 2010b), hence it was considered important to assess maternal fetal bonding as a possible predictor of impaired mother to infant bonding.

As described in Chapter1, the terms 'attachment' and 'bonding' are often used interchangeably in the psychology literature. However, it has been suggested that when these terms are used with the fetus during pregnancy, bonding best describes the feelings of the women towards the unborn child and attachment describes the relationship of an infant towards its mother (Ji et al., 2005). Moreover, due to the lack of reciprocity between the woman and the fetus in pregnancy, the meaning of the term 'attachment', as defined by (Bowlby, 1969) cannot be transferred to the antenatal period (Van den Bergh and Simons, 2009, Walsh, 2010). Nevertheless, a number of instruments measuring the mother-fetal relationship have used the term 'attachment', e.g. the Maternal Foetal Attachment Scale (Cranley, 1981), the Maternal Antenatal Attachment Scale (Condon, 1993) and the Prenatal Attachment Scale (Muller, 1993).

The Maternal Antenatal Attachment Scale (Condon, 1993), was selected to measure maternal fetal bonding because it focuses exclusively on the thoughts

and feelings about the fetus which essentially measures the same construct as the definition of mother to infant bonding used in this study.

The MAAS (appendix 32) is a 19-item self-report questionnaire, developed to measure the quality of maternal attachment to the unborn child. Factor analysis yielded two distinct factors, namely, quality of attachment ("quality"; 11 items), and time spent in attachment mode, thus indicating pre-occupation with the fetus ("time spent"; 8 items) (Zimerman, 2003, Van den Bergh and Simons, 2009). It was validated through item analysis where the 19 retained items achieved a high internal consistency, with a Cronbach's alpha of 0.82 (Condon, 1993). Other studies have found different Cronbach's alpha scores of 0.69 (Schwerdtfeger and Goff, 2007), $\alpha \geq 0.70$ (van Bussel et al., 2010a) and $\alpha > 0.80$ (Condon and Corkindale, 1997, Laxton-Kane and Slade, 2002).

In the current study, women were asked to complete the MAAS at 36 weeks gestation. Responses are given using a 5-point rating scale, with a score of 1 representing absence of feelings towards the fetus and one of 5 indicative of very strong feelings. The minimum score for the total MAAS is 19 and the maximum 95, with higher values indicating good fetal bonding. The scores for the 'quality' sub-scale range between 11 and 50 and 'time spent' between 8 and 40. High scores reflect respectively a positive quality of attachment and a high pre-occupation with the fetus. This scale has no established threshold cut-off for high and low fetal attachment categories however score of 76 for the total maternal attachment score, a mean scores from (Condon, 1993) has been used in two studies (Pollock and Percy, 1999, Hart and McMahon, 2006) as cut-off for constructing fetal attachment categories. In the current study,

similar score ≥ 76 on maternal antenatal attachment total was used to categorise participants as “high” while score ≤ 76 was rated as low fetal bonding.

3.5.1.5 Assessment of maternal personality disorder

The association between maternal personality disorder and postnatal depression is well documented (Johnstone et al., 2001, Robertson et al., 2004, Verkerk et al., 2005, Milgrom et al., 2008, Klein et al., 2009, Jones et al., 2010, Gelabert et al., 2012). As maternal postnatal depression is a significant risk factor for poor mother to infant bonding, it is possible that maternal personality disorder could affect mother-infant bonding perhaps through an indirect effect of postnatal depression. In addition, the presence of maternal personality disorder has been shown to have a significant effect on infant care and maternal involvement with the infant (Conroy et al., 2010). In a recent review, Laulik et al. (2013) identified parental personality disorder as a risk factor for a disturbed parent infant relationship. Hence assessment of maternal personality disorder was considered relevant in the current study.

Maternal personality disorder in the current study was assessed at 36 weeks gestation and six weeks postnatally using the Standardised Assessment of Personality Abbreviated Scale (SAPAS) (Moran et al., 2003), (appendix 33). This questionnaire consists of nine items describing personality disorder. A score of 3 on the screening interview correctly identifies the presence of DSM-IV personality disorder in 90% of participants with a sensitivity and specificity of 0.94 and 0.85, respectively (Moran et al., 2003). It has been validated for

patients with a first episode of depression (Bukh et al., 2010) and other clinical samples (Germans et al., 2008, Hesse and Moran, 2010). However, it has not yet been validated for the perinatal period, although it has been used by perinatal researchers (Conroy et al., 2010, Conroy et al., 2012).

Women were asked to answer yes or no to the 8 item questions (yes=1; no=0), with the total score ranging from 0 to 8 and a high score indicating presence of personality disorder. A cut-off score of 4 was recommended by (Germans et al., 2008) as correctly classifying 81% of the patients with personality disorder, validated with DSM-IV personality disorder by these researchers, which is different from a score of 3 suggested by the original study (Moran et al., 2003).

3.5.2 Primary outcome measure

3.5.2.1 Assessment of mother-to-infant bonding

The primary outcome measure was impaired mother-infant bonding as measured by the Mother Infant Bonding Scale (MIBS) (Taylor et al., 2005), (appendix 34). Researchers have previously investigated the mother-infant relationship using video recordings to provide direct observation of mother to infant interaction (Anisfeld and Lipper, 1983) in hospital and home settings. Clinical interviews have also been used for diagnostic purposes (Brockington, 2006), however, these methods can be expensive and require trained psychiatrists to assess the women (van Bussel et al., 2010b). In addition, a range of instruments have been used to assess the relationship between a mother and her infant, including: The Bethlem Mother-infant Interaction Scale

(BMIS), (Kumar and Hipwell, 1996), the Maternal Behavioural Observational Scale (Cernadas et al., 2003), the Parental Stress Index Scale (Else-Quest et al., 2003), the Yale Inventory of Parental Thoughts and Action (Feldman et al., 1999), and the Bethlehem Mother-infant Interaction Scale (Pearce and Ayers, 2005) .

These instruments focus on maternal interaction with the infant more than the woman's emotional feelings towards it. It has been argued that measures of maternal affection using behavioural tools makes no provision for maternal behavioural style, as a woman's previous experience with children, her culture or religious beliefs could influence her current behaviour with her infant. In other words, the behaviour observed in some mother-to-infant relationship assessments (video tape recordings or maternal behavioural questionnaires) could be an indicator of the woman's fatigue or cultural differences rather than maternal affection (Muller, 1994, Condon and Corkindale, 1998).

Other self-rating questionnaires used to screen early mother-to-infant bonding problems include: The Maternal Attachment Inventory (MAI) (Muller, 1994), the Maternal Postpartum Attachment Scale (MPAS), (Condon and Corkindale, 1998) and the PBQ (Brockington et al., 2001). The PBQ (Brockington et al., 2001) and the MIBS (Taylor et al., 2005) are the two most cited and validated scales for measurement of early mother-infant bonding as described in the previous chapter. The reliability and validity of these two questionnaires as measured using the same construct of impaired bonding have been supported by Wittkowski et al. (2007 and VanBussel et al. (2010). The most widely used

validated scale for assessment of impaired mother-infant bonding in the literature is the PBQ, however, this is long (26-items), with four different subscales (rejection, anger, anxiety and risk of abuse). In addition, it was originally developed for a population of women with psychiatric disturbance.

The MIBS was designed for use with postnatal women in the general population and is short and easy to use. It has been well validated and when compared with the PBQ was found to measure the same construct (Wittkowski et al., 2007, van Bussel et al., 2010b). (Taylor et al., 2005) It can be used from the first week of birth.

The questionnaire consists of eight adjectives (loving, resentful, neutral or felt nothing, joyful, dislike, protective, disappointed and aggressive), each followed by a four-point Likert scale ranging from “Very much” (0) to “Not at all” (3). When the adjective reflects a negative emotional response, the scoring is reversed, with possible scores on the MIBQ ranging between 0 and 24, with high scores indicating a poor mother-to-infant bond. Studies of test-retest reliability and construct validity show reasonable internal consistency, (Cronbach’s alpha) of 0.55 (Wittkowski et al., 2007), 0.75 (Figueiredo et al., 2009) and 0.67 (van Bussel et al., 2010b).

The questionnaire includes two parts which require ratings on the same items, the first covering maternal feelings towards the infant in the “first week” post birth (retrospective), while part two covers maternal feelings “now” (six weeks postnatal). Hence, the participants would have two bonding scores, one in the first week postnatal ranging from 0 to 24 and one at six weeks postnatal also ranging from 0 to 24. The mother-infant bonding score at six weeks postnatal

was used as the outcome measure as maternal feelings towards infants may develop progressively as described previously (Taylor et al., 2005, Wittkowski et al., 2007, van Bussel et al., 2010b), with potential for possible recall bias if the score for the first postnatal week was used. A cut-off score of 2 and above was used as this has been validated using clinical interviews (Bienfait et al. 2011). A summary of study measures administered and when, is presented in table 3.1.

Table 3-1 Summary of Study Measures Administered at Time 1 (Antenatal) and Time 2 (Postnatal)

Psychometric Measures	Time 1: late pregnancy - (average 36 weeks gestation)	Time 2: 6 Weeks Postnatal	
			First week Retrospective
Mother-Infant Bonding Scale (MIBS) (Outcome)		X	X
Antenatal Attachment / Maternal Fetal Bonding (MAAS)	X		
Antenatal Depression (EPDS)	X	X	
Spielberger State Anxiety	X	X	
Spielberger Trait Anxiety	X	X	
SAPAS Personality Disorder	X	X	
Stressful Life Events Scale	X	X	
Clinical history was screened at recruitment and using clinical records			

3.6 Potential confounding, mediating or moderating variables

A confounding variable is defined as a variable which is a predictor of the outcome variable but it is also associated with the risk factor or exposure variable (Bauman et al., 2002, Katz, 2006). A *mediator* variable is a variable

with a causal link between an independent variable and how it affects the outcome variable whereas a *moderator* variable increases or decrease the effect of the independent variable on the outcome (Baron and Kenny, 1986, Kraemer et al., 2002, Fairchild and McQuillin, 2010).

3.6.1.1 Socio-demographic data

The following socio-demographic data were collected from women on study entry:

- **Maternal age.** This was treated as a continuous variable and also categorised into four age groups ('17-24', '25-30', '31-35' and '36-44' years) to aid the analyses.
- **Marital status** categorised as single, married or living with a partner.
- **Self-assigned ethnicity.** Participants selected their ethnicity from one of the following categories: (White, Black, Asian, mixed ethnic group, and other ethnic groups), based on the Office for National Statistics (ONS, 2011) (Appendix 25).
- **Indicators of maternal socioeconomic status (SES)** was assessed by maternal educational attainment (first categorised into: none, General Certificate of Secondary Education (GCSE), A-level, university degree and above), based on the UK education system; employment status (full-time/part-time/unemployed /housewife/ student) and occupation (professional, managerial, skilled/unskilled, and other), based on the Classification of Occupation (HMSO, 1980) (Chandola, 2000).
- Participants were classed as of higher socio-economic status if they had a university degree, were in a professional or managerial occupation, or in full or part-time employment as a proxy of their income (Braveman et

al., 2005). Women who did not meet these criteria were classed as of lower socio-economic status.

- **Country of birth.** This was included as it is possible that there may be cultural differences in the way mother to infant bonding is viewed, and practiced, in different countries.
- **Parity** was categorised into two categories: (1) Primiparous for women giving birth to their first child, and (2) 'multiparous' for those having their second or subsequent child.
- **Smoking status and alcohol intake in pregnancy.** Maternal smoking status during pregnancy was obtained by asking the women 'Are you currently smoking?' with a dichotomous 'yes' or 'no' response. A similar question was asked regarding alcohol intake; with women who indicated that they currently drank alcohol being asked to estimate their weekly alcohol intake using the prompt 'one unit is equivalent to a small glass of wine/a glass of beer'. However, due to the small number of women who reported alcohol intake in pregnancy, responses were categorised into a dichotomous 'yes' or 'no', rather than reported quantities consumed.

Other variables identified in the literature as potential moderator of mother-infant bonding included: social support pregnancy, labour and birth outcomes; neonatal outcomes and breastfeeding. These variables were measured in the current study to assess their associations with impaired mother to infant bonding.

3.6.1.2 Social support

Information on the women's living arrangements was used as an indicator of their social support. Participants were asked on recruitment to indicate if they lived with their husband, partner, parents, and other family members or if they lived alone.

3.6.1.3 Pregnancy complications

A high risk pregnancy may impact on a woman's pregnancy outcomes and her birth experiences, which could subsequently increase her risk of anxiety or depression (Maloni et al., 2005, King et al., 2010), resulting in impaired mother to infant bonding. Pregnancy complications were categorised into high and low risk according to the (NICE, 2008a) antenatal guideline. Those participants with pre-existing health conditions (e.g. cardiac disease, diabetes, asthma, multiple sclerosis, high blood pressure, psychiatric illness) or problems diagnosed in pregnancy (e.g. obstetric cholestasis, essential high blood pressure, pre-eclampsia, gestational diabetes, placenta-previa, antepartum vaginal bleed, deep vein thrombosis, preterm labour) were classified as high risk, and women with no conditions considered a threat to the health of the woman or the fetus classified as low risk.

3.6.1.4 Labour, birth and neonatal outcomes

Labour, birth and neonatal outcomes data were obtained from a combination of maternal self-report and maternal electronic obstetric records using study postnatal data collection form (appendix 27) and neonatal data collection form (appendix 28). Three indicators were used to assess labour and birth outcomes.

These includes: pain relief in labour, mode of delivery and birth complications up to 24 hours post-delivery in mother and baby.

3.6.1.5 Pain in labour

It has been suggested that pain in labour has a negative effect on mother infant bonding (Ballard et al., 1995, Kumar, 1997), although other researchers (Weisman et al., 2010) have reported that this has a positive effect on maternal attitudes towards their infants. Pain in labour was assessed in this study to test a potential association with mother infant bonding. Women were asked at six weeks postnatal to recollect and rate their experience of labour and birth pain on a five point scale, “no pain” (0) to “extremely painful” (5).

3.6.1.6 Use of labour pain relief

Pain relief in labour was initially divided into five categories: no pain relief, entonox inhalation, pethidine injection, epidural and general anaesthesia. As there were so few women in categories other than epidural, labour pain relief was categorised into no epidural and epidural analgesia for the purposes of analysis.

3.6.1.7 Mode of birth

Mode of birth has been linked with disturbance in early mother to infant bonding in terms of having a negative birth experience, (DiMatteo et al., 1996, Herishanu-Gilutz et al., 2009, Weisman et al., 2010). It was important to include

this to test for any possible association with early mother to infant bonding. Information on mode of birth was obtained through maternal self-report and verified from obstetric records. It was categorised into spontaneous vaginal delivery (SVD), instrumental delivery (either forceps or ventous delivery), elective caesarean section and emergency caesarean section.

3.6.1.8 Birth complications

Information on maternal and neonatal complications at birth was obtained from the obstetric records. Birth complications included postpartum haemorrhage (defined as estimated blood loss of more than 1000m/ls) after delivery, third or fourth degree perineal tear or a perineal tear repaired in theatre.

3.6.1.9 Neonatal outcome

Infant health status could be a potential factor that influences maternal behaviour towards the infant (Conde-Agudelo et al., 2003), meaning an adverse neonatal outcome could have a negative effect on mother to infant bonding. Gestational age at birth, infant birth weight, Apgar score at one and five minutes, neonatal intensive care admission and neonatal abnormalities, were collected from the obstetric records. These outcomes were divided into two categories: (1). neonatal complications including low infant Apgar score at birth (<4), neonatal abnormality, admission to the neonatal unit, gestation \leq 36 weeks, and low birth weight <2000g and (2) no neonatal complications.

3.6.1.9.1 Infant feeding

Infant feeding was included because previous studies have identified breastfeeding as a potential factor that promotes mother infant bonding (Cernadas et al., 2003, Else-Quest et al., 2003, Kim et al., 2011). Information on maternal feeding following the birth was obtained from maternal discharge hospital records. The women were first asked to indicate how their infants were fed at six weeks postnatal (“exclusive breast-feeding”, “bottle-feeding”, and “mixed-feeding”). If their answer was exclusive breastfeeding, they were then asked to indicate when they initiated it (“0-1 hour”, “1-4 hours”, “5-24 hours” >24 hours) post-delivery.

3.7 Validity and reliability of self-reported scales

The instrument validation techniques used in quantitative research include factor structure, construct validity, face validity, discriminant validity, divergent and convergent validity and reliability (e.g., test-retest, internal consistency, inter-rater reliability). Good validity and reliability of scales is crucial to the conduct of high quality research (Kimberlin and Winterstein, 2008).

Validity refers to the extent to which an instrument accurately measures what it is intended to measure. Reliability of a scale refers to its ability to measure constantly (Tavakol and Dennick, 2011). Internal consistency (using Cronbach’s alpha) is a form of reliability which assesses the consistency of the question items within a scale/subscale. The extent to which responses are consistent

indicates whether the items are measuring the same underlying construct. Cronbach's alpha is a measure of the internal consistency of a scale, and is the most common index of a scale's reliability (Pallant, 2010, Tavakol and Dennick, 2011). According to Gliem and Gliem (2003), p.88, it is important to calculate and report the Cronbach's alpha coefficient value for internal consistency reliability in any new or standardised Likert-type scales or subscales used in research studies. Cronbach's alpha coefficients range from 0 to 1, and the minimum threshold for acceptable reliability is α of 0.7 (Gliem and Gliem, 2003, Streiner, 2013). High quality standardised scales used in research and clinical assessment typically have high reliability alphas above 0.9, (Yang and Green, 2011).

Table 3.2 compares the Cronbach's alpha coefficient scores of all self-report scales used in this study with the validity and reliability of the same scales as reported from previous literature. Overall, the self-report scales used in this study (i.e., State-Trait Anxiety Inventory, Stressful Life Events Questionnaire, EPDS, MAAS, and MIBS) had acceptable Cronbach's alpha values ($\alpha \geq 0.7$), (Bland and Altman, 1997), demonstrating good internal consistency comparable with those reported in the extant literature. However, the internal consistency of the Standardised Assessment of Personality-abbreviated scale (SAPAS) was low ($\alpha = 0.46$ and 0.48) in this study.

Table 3-2 Psychometric qualities of scales used in the current study

Scales	Author	Participants	Validity tests in previous studies	Reliability tests in previous studies	Reliability (Cronbach's alpha) in current study
				Internal consistency (α)	Internal consistency:
STAI-State-Trait Anxiety Inventory	Spielberger (1983)	General population		Test-retest $r=0.86$	Antenatal: $N=301$ State-anxiety $\alpha =0.92$ Trait-anxiety $\alpha =0.91$.
	(Grant et al. (2008))	Third trimester of pregnancy and 32 weeks postnatal $N=100$	Predictive validity (cut off 40) Sensitivity:81% Specificity:80%	Antenatal $\alpha =0.95$ Postnatal: $\alpha =0.94$	Postnatal : $N=226$ State-anxiety $\alpha =0.94$ Trait-anxiety $\alpha =0.93$.
S L E Q	Bergman et al. (2007)	-	no validation		Antenatal: $\alpha =76$ Postnatal: $\alpha =66$.
EPDS		Postnatal	Predictive validity	Split-half reliability:	Antenatal EPDS:

Scales	Author	Participants	Validity tests in previous studies	Reliability tests in previous studies	Reliability (Cronbach's alpha) in current study
				Internal consistency (α)	Internal consistency:
MAAS	Cox et al. (1987)	women No=84	(cut off 12.5) Sensitivity:86% Specificity:78%	r= 0.87	α =0.84
	Cox et al. (1996)	Non Postnatal women	Predictive validity (cut off 12.5) Sensitivity: 79% Specificity: 85%		Postnatal EPDS: α =0.87
	(van Bussel et al. (2010a))	N=298			N=301
	MAAS (total)	8-15 weeks		α = 0.79	
		20-26 weeks		α = 0.80	
		30-36 weeks		α = 0.78	α = 0.81
	Quality subscale	8-15 weeks		α = 0.73	
		20-26 weeks		α = 0.73	
		30-36 weeks		α = 0.69	α = 0.71
	Pre occupation	8-15 weeks		α = 0.76	

Scales	Author	Participants	Validity tests in previous studies	Reliability tests in previous studies Internal consistency (α)	Reliability (Cronbach's alpha) in current study Internal consistency:
SAPAS	Subscale				
		20-26 weeks		$\alpha = 0.77$	
		30-36 weeks		$\alpha = 0.73$	$\alpha = 0.69$
	(Moran et al. (2003))	Psychiatric patients	No perinatal validation Predictive validity (cut- off 3) Sensitivity: 94% Specificity: 85%		Internal consistency Antenatal: $\alpha = 46$ Postnatal: $\alpha = 48$
	(Germans et al. (2008))	SCID-II (First et al., 1997) Psychiatric patients SCID-II (Beck, 1995)	Predictive validity (cut- off 4) Sensitivity: 83% Specificity: 80%		
MIBS	(Bienfait et al. (2011))	Postnatal 2-3 days	Predictive validity (cut off 2) Sensitivity: 90% Specificity: 80%		N=226
	(Taylor et al. (2005))	Postnatal 12 weeks		$\alpha = 0.71$	
	(Wittkowski et al. (2007))	Postnatal 2nd day		$\alpha = 0.55$	
		3rd day		$\alpha = 0.49$	

Scales	Author	Participants	Validity tests in previous studies	Reliability tests in previous studies	Reliability (Cronbach's alpha) in current study
				Internal consistency (α)	Internal consistency:
	(van Bussel et al. (2010b))	N=263			
		8-12weeks		α =0.67	1 st week: α =0.79
		20-25 weeks		α =0.58	6 weeks: α = 0.53
Abbreviations: STAI=Spielberger State-Trait Anxiety Inventory; S L E Q= Stressful Life Event Scale; EPDS = Edinburgh Postnatal Depression Scale; SAPAS= Standardised Assessment of Personality Abbreviated Scale; MAAS= Maternal Antenatal Attachment Scale; MIBS= Mother Infant Bonding Scale					

3.8 Study Population and Setting

Participants were recruited from a non-probability (non-random) purposive sample consisting of pregnant women between 28 and 40 weeks gestation who attended the antenatal clinic or day assessment unit one NHS hospital in West London. As the researcher was temporarily working there as a research assistant, it was easier to access and recruit women who met study inclusion criteria. A single site was chosen because a multi-centre site study was not possible due to limited funding and the researcher who was responsible for all aspects of this study studying and working on a part-time basis.

The data were collected over a four year period from 2008-2012. The four year period was to achieve the required sample size due to the researcher undertaking her studies on a part-time basis. The selected hospital is a tertiary referral maternity unit with extensive high-risk services for women with complicated pregnancies, such as women with pre-existing diabetes or cardiac disease, as well as midwifery-led services for women with uncomplicated low risk pregnancies. The hospital also provides one-to-one midwifery care for vulnerable and disadvantaged women within their geographical area i.e., women who are refugees and asylum seekers, those who live in poverty, homeless, or live under the threat of domestic violence (House of Commons Health Committee, 2003) . One-to-one midwifery is a system piloted in this hospital in 1993 where one midwife provide midwifery care to a case load of women thorough out their pregnancy, birth and up to one month after birth (McCourt et al., 1998). Women between 28 and 40 weeks gestation and attending the antenatal clinic or day assessment unit at the study site were

approached by the researcher and those eligible were invited to take part. To recruit women from the one-to-one midwifery group a substantive ethics amendment was required so that women could be recruited in their own homes and not the hospital clinic, (appendix 10 and 11).

3.9 Inclusion and exclusion criteria

The original aim of this study was to determine antenatal predictors of poor mother-infant bonding in healthy women with a low risk first pregnancy, thereby excluding both multigravida and women with a high risk pregnancy. After the first six months of recruitment, a revision was made to the recruitment inclusion criteria, as it was considered of interest to also explore the effects of high risk pregnancy on mother-infant bonding. This decision was made following new evidence published by King et al., (2010) who conducted a study in the same study site as the current research, which found higher depressive and anxiety symptoms in women with medical disorder of pregnancy. As high risk pregnancy could affect any woman, it was important to include primgravida and multigravida women in this study. Data collected in the first six months of recruitment were combined with the new recruits following this amendment. This substantive amendment to the study protocol was approved by the ethics Committee; amendment number 2, (appendix 12 and 13).

Following this revision, the study inclusion and exclusion criteria included:

Inclusion criteria

1. *Women who had a singleton pregnancy*
2. *Primgravida and multigravida women*
3. *Women whose pregnancies were between 28 and 40 weeks gestation, who attended the antenatal clinic or day assessment unit at the study site*
4. *Women who received home based antenatal care as part of a one-to-one midwifery group*
5. *Women with complicated pregnancies, including pre-existing and medical complications diagnosed in pregnancy.*
6. *Women able to read and understand English*
7. *Women aged 17 years of age and over*
8. *Women of any ethnicity*

3.9.1.1 Exclusion criteria

1. *Women who had a twin pregnancy*
2. *Women unable to read and understand English*
3. *Women aged less than 17 years of age*
4. *Women currently receiving psychiatric treatment*
5. *Women who had a stillbirth in current pregnancy.*

3.10 Sample size

The sample size for this study was 300 participants, which allowed for loss to follow up (estimated at around 15%) and women who may have not met inclusion criteria due to pregnancy loss or premature birth (estimated at around 10%). Of the total cohort of 300 women, it was expected that the final study sample would include approximately 225 participants.

The sample size estimation was based on a combination of four previous relevant studies (Glover et al., 1994, Taylor et al., 2005, O'Higgins et al., 2013). Based on the findings of (Glover et al., 1994), it was estimated that approximately 45 women (15%), would score above the threshold for probable major depression (EPDS >13), in late pregnancy, and approximately the same number at six weeks postnatal. The results of the other two studies (Taylor et al., 2005; O'Higgins et al., 2013), using the EPDS (Cox et al., 1987) and MIBS (Taylor et al., 2005) found that 40%–55% of women in the depressed group also scored above the threshold for poor mother-infant bonding as compared with 15–20% of those in the non-depressed group.

3.10.1.1 Sample size calculation

Using the information given above: if 225 eligible women were available for the study, then it was expected that 15% (n=34) would be depressed. It was also assumed that a proportion of 15% of non-depressed women would have poor mother-infant bonding and a proportion of 40% of depressed women would have poor bonding (odds ratios=3.7), then the study would have a power of 90% to detect a significant difference with a 1-sided Fisher's Exact test at a

significance level of $p < 0.05$. The sample size calculation was performed using NCSS PASS (HINTZE, 2001) by the Statistical Advisory Service at Imperial College London (see appendix 3). Ultimately a higher number of women were recruited ($n=461$) to achieve the desired target of 225 due to a higher than expected rate of attrition. This is discussed further in Chapter 5.

3.11 Recruitment

Each prospective participant was approached by the researcher. To ensure they met study inclusion criteria, prospective participants were asked relevant questions about their health and pregnancy. The study protocol was explained to the one-to-one midwives to ensure they were able to refer potentially eligible women under their care. A study information leaflet (appendix 8) was offered to all potential participants, which included the researcher's contact details and the women were encouraged to ask the researcher any questions about the research.

Those who wished to take part were either recruited on the day contact was made or during their next antenatal appointment, if they wished to give more thought to their participation in the study. If a woman was willing to participate, she was asked to complete a study consent form (appendix 14) and issued with a unique study reference number to maintain her confidentiality and anonymity. A copy of the signed consent form was given to the woman and another copy included in the woman's obstetric records. A letter was sent to each participant's General Practitioner (GP) (appendix 17) with the woman's permission to inform him/her of the woman's participation in the study. A demographic data collection form (appendices 25 and 26) was completed by

women following recruitment to obtain information on maternal age, ethnicity, and level of education, parity, smoking status, alcohol consumption, and any medical problems, such as pre-eclampsia, diabetes, obstetric cholestasis before or during this pregnancy.

The recruitment process was slightly different for women who received one-to-one group care. In these cases, a letter was sent to each one-to-one midwife in the hospital informing them about the study and their assistance in recruiting women in their caseload, (see appendix 15). A study leaflet (appendix 16) was offered to women by their one-to-one midwife. If any of the women were willing to take part in the study, the researcher was contacted by the midwife and would visit women at home with their one-to-one midwife to provide any further information about the study and obtain the woman's informed consent if they wished to participate.

3.12 Data collection and data management

3.12.1 Data collection process

Women recruited were asked to complete two self-administered questionnaires, namely Time 1 (late pregnancy between 36-40 weeks gestation) and Time 2 (six weeks postpartum).

A Time 1 questionnaire pack was mailed to women who had consented to take part at 36 weeks gestation. On average, the antenatal study pack was sent to women four weeks following recruitment except if they were recruited after 36

weeks, when the pack was given to them to complete in the clinic or posted the same week. The pack included a covering letter (appendix 18), a copy of each antenatal questionnaire and freepost return envelopes. The antenatal questionnaire contained a self-report questionnaire to assess maternal anxiety, depressive symptoms, stress, personality traits and maternal fetal bonding.

A second questionnaire pack (postnatal questionnaire), also with freepost return envelopes was sent to the women between four to five weeks after delivery with a covering letter (appendix 18) to be completed six weeks after giving birth. This was only sent to women who had completed the antenatal questionnaire. The postnatal pack contained the same measures as the antenatal questionnaire, other than that the Maternal Antenatal Attachment Scale for fetal bonding was replaced with the MIBS, which was the primary outcome measure. A postnatal data collection form (appendix 27) was also included in the postnatal pack to collect data from women on their experience of pain of labour, use of pain relief in labour, and infant feeding at 6 weeks.

3.13 Ethical considerations

All study participants were assured of confidentiality and anonymity regarding any data they provided. Moreover, it was stressed on the information sheet (appendix 8 and 9) and during recruitment that the women had the right to decline to participate, and a right to withdraw from the study at any point, which would not have any impact on the care they received; and if they did provide

consent, that they could ask for more explanation at any stage of the study. Participation was entirely voluntary, with no financial remuneration. All participants were treated with dignity and respect and there were no potential risks of harm to either the women or the researcher.

3.14 Study adherence and loss to follow up

Low response rates reduce the effective sample size and can introduce nonresponse bias. If non-respondents differ significantly on characteristics or measures used, it could affect the external validity of a study (Edwards et al., 2007). To minimise the non-response rate, the women were contacted before sending out the questionnaires (by phone, text or email) at Time 1 and Time 2. A reminder letter (see appendix 21 and 22), was sent to women if questionnaire has not been returned after two weeks of sending out the questionnaire pack. Participants were also contacted again by text if no questionnaire had been returned after a week of sending out a reminder letter.

3.14.1 Data entry and cleaning

Women's baseline (Time 1) and pregnancy outcome data (Time 2) were manually entered into an SPSS database by the researcher. Questionnaire data were also manually entered into SPSS by the researcher, with the support of two research assistants based at the study site. The composite scores for all questionnaire scales were automatically calculated by the syntax formulae in SPSS. The database was updated regularly until all complete questionnaires were received.

To check the quality of the data entry, the data set was checked for errors using the descriptive statistics analysis in SPSS for each variable in order to highlight inconsistencies. Scores outside the range of possible scores on measures used were corrected or removed if entered in error. Outliers were re-examined by recalculating the scores of the variable of interest. Finally, 10% of the questionnaire data (n=30) were randomly selected, entered again and the SPSS file rechecked for quality and consistency in data entry by the researcher.

3.14.2 Dealing with missing data

A full report of missing values was completed for each variable. Missing data were found for a number of study variables. Reasons identified included return of an incomplete questionnaire at Time 1 and Time 2. Some women declined to complete questionnaires either at Time 1 or Time 2 (non-responders). Missing data are common in observational and experimental studies (Lee and Simpson, 2014), however, the degree to which missing data becomes problematic depends on the pattern and amount of missing values (Kim and Bentler, 2002, Little and Rubin, 2002). Less than two percent of missing data was due to incomplete questionnaire completion at Time 1 and Time 2. For the purpose of analysis pair wise deletion was performed for missing data with advice from the statistician based at King's College London (KCL). Excluding cases pairwise was considered the best option of dealing with missing data, as cases were excluded if data required for pre-specified analysis were missing.

3.15 Data analysis

Data analysis was undertaken using IBM SPSS version 20, with statistical advice provided by a statistician at KCL.

3.15.1.1 Univariate analysis

Descriptive statistics were performed on continuous and categorical variables, to understand the variability in the data and frequency of demographic and pregnancy-related characteristics. To assess distribution of continuous data, a normal probability (P-P plot) was derived to determine if data followed a normal distribution (Tanyildizi, 2011). Visual examination of histograms of frequency distribution was used to assess patterns of data distribution. Three measures (Stressful Life Event Scale, MIBS and EPDS) were non- normally distributed with positive skewness (cluster of scores to the left at low values), while others measures (MAAS and STAI), showed a reasonable normal distribution. Parametric analysis was used when data were normally distributed and nonparametric tests where data were non-normally distributed.

A number of variables collected were multi-categorical, however univariate analysis found a small number of cases for some categories. Through consultation with the statistician, a decision was made to combine some categories to obtain reasonable values for purposes of analysis. These included; living arrangements (living with husband/partner, alone or other); maternal educational attainment (none/O'levels/GCSE), ('A 'levels/ vocational training equivalent); (university degree BSc, Masters/ PhD), maternal

occupation (professional, managerial, skilled/unskilled, other), pain relief in labour and birth (epidural and non-epidural analgesia).

3.15.1.2 Bivariate analysis

Bivariate analysis was used to explore relationships between the primary outcome (mother-infant bonding status) and independent variables. Parametric t-tests were used where the normality assumption was satisfied and non-parametric Mann Whitney U test where violated. As explained above, a number of maternal socio-demographic variables were considered to be potential confounders. To identify if any of the maternal socio-demographic variables in the current study were operating as confounders, the association between maternal socio-demographic variables, including maternal age, ethnicity, education, occupation, parity, smoking and alcohol consumption and mother to infant bonding, were investigated using the chi-squared test for independence. If any variables were associated with mother-to-infant bonding, it was considered to be a confounder that needed to be controlled for in further analyses. More specifically, a number of variables including maternal obstetric high risk status, mode of delivery, pain of labour, mode of pain relief in labour, neonatal outcome, method of infant feeding, and social support, were considered as potential mediators of poor mother-to-infant bonding. A Chi-square test for independence was first performed with each variable to explore a possible association with mother-to-infant bonding status.

3.15.1.3 Logistic regression

Series of logistic regression analysis was used to address the first study research question, namely, *Does depression or other psychological problems in late pregnancy predict poor mother-to infant bonding at six weeks postnatal?*

To assess the relative contribution of individual variable in predicting the outcome variable, a series of logistic regression analyses were conducted. Logistic regression was appropriate as the outcome variable was a binary variable with two categories: good bonding (score <2) and poor bonding (score ≥2). Logistic regression analysis is used to see which predictor variables predict membership in one category or another (in this case good or poor bonding), and predictor variables can be categorical or continuous. Therefore, this approach allowed for inclusion of all statistically significant variables identified using bivariate analysis, and investigate the influence of each as a predictor of the mother–Infant bonding score at six weeks postpartum.

Logistic regression analysis was also used to answer the second research question namely; *do psychometric measures of postnatal anxiety or depression correlate with the Mother to Infant Bonding Scale?*

The researcher sought to compare data from women with a high risk pregnancy with those with low risk pregnancy, to answer the third research question ‘*does having high obstetric risk in pregnancy affect mother-to-infant bonding?*’ Consequently, as these data were skewed, a Mann-Whitney U Test was performed to compare the mean rank scores of antenatal and postnatal psychometric measures among women with high and low risk pregnancy.

3.16 Chapter summary

This chapter has described, explained and justified the aim, objectives and method of the study. As described, a prospective cohort study was undertaken to explore antenatal predictors of impaired mother-infant bonding, among women recruited in one West London Hospital. As well as to explore the feasibility of using biological measures of stress during pregnancy to predict impaired mother-infant bonding six weeks postnatal on a subset of participants in the same cohort as a pilot study. This pilot study will be presented in the next chapter.

CHAPTER 4 NESTED PILOT STUDY

4.1 Background

The hypothalamic-pituitary-adrenal (HPA) axis is one of the major systems involved in stress response and its regulation. The HPA system is activated during stress and threat, and studies have looked at the concentration of its end product, the stress hormone cortisol as a biomarker of psychological stress (Hellhammer et al., 2009, Buitelaar, 2013, Nater et al., 2013). Non-invasive assessment of biomarkers in saliva has created opportunities to study how biological and social processes interact to influence health and human behaviour. Studies have found a significant direct relationship between the concentration of plasma cortisol and saliva cortisol (Kirschbaum and Hellhammer, 1994, Levine et al., 2007), hence saliva samples are an established way of measuring the concentration of cortisol, which has long been used in human psychobiological studies as a biological marker of stress, anxiety and depression (Obel et al., 2005, Kivlighan et al., 2008, Bolten et al., 2011). The association between mood symptoms and altered cortisol secretion has been shown in some studies but not consistently in non-pregnant adult (Knorr et al., 2010, Vammen et al., 2014) as well as in pregnant population (O'Connor et al., 2014).

The sympathetic nervous system (SNS) is another major system thought to play a role in stress response in the period immediately following the onset of the stressor (Ali and Pruessner, 2012). In recent years salivary alpha amylase has been used as a non-invasive surrogate marker for the sympathetic activity, a component of the stress response (Schumacher et al., 2013). Although salivary

alpha amylase is a digestive enzyme mainly involved in the breakdown of starch molecules in the oral cavity and not a direct by-product of the SNS (Hellhammer et al., 2009, Ali and Pruessner, 2012, Baibazarova et al., 2013). However, several studies have found elevated levels of salivary alpha amylase under physical and psychological stress conditions (Gordis et al., 2006, Granger et al., 2007, van Stegeren et al., 2008, Nater and Rohleder, 2009, Nater et al., 2013).

Antenatal salivary cortisol and alpha amylase concentrations, which are thought to reflect levels of maternal anxiety, stress and depression during pregnancy in some studies, could be used to predict poor mother-infant bonding, because antenatal depression or anxiety is considered a risk factor for impaired mother-infant bonding (Figueiredo and Costa, 2009).

Moreover, maternal behaviour and responsiveness to the infant has been positively associated with higher maternal cortisol levels during the early postpartum period in human studies (Fleming et al., 1997, Giardino et al., 2008). Cortisol and alpha amylase have also been implicated in maternal bonding in non-human populations. That is, there is evidence from animal studies that parturition promotes a range of hormonal and other biological changes in the mother which facilitate maternal behaviour (Bardi et al., 2004). For instance, a high cortisol level in late pregnancy was found to predict worse mother-infant bonding in baboons (Bardi et al., 2004). On the other hand, Kivlighan and Granger (2006) found low salivary amylase was associated with reduced bonding in other contexts.

To the author's knowledge, no published study has yet examined the association between these two hormones (i.e., salivary alpha-amylase and cortisol) during the perinatal period and mother-infant bonding. The present pilot study investigated this association.

4.2 Aim and objectives of pilot study

The aim of the pilot study was to collect and analyse two biological measures of stress (i.e., cortisol and alpha-amylase) during pregnancy to identify women at risk of developing early mother-infant bonding problems postnatally. The findings from this formative research would be used to evaluate feasibility and effect size for future research in this area.

Specific objectives:

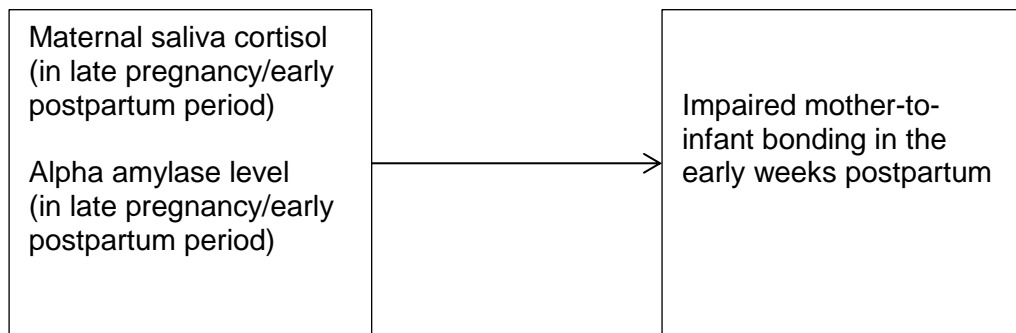
The specific objectives of the pilot study were:

- To explore if raised maternal salivary cortisol and salivary alpha – Amylase in late pregnancy, or during the postnatal period, are associated with poor mother-infant bonding in early weeks postpartum.
- To assess the feasibility of conducting a future larger study using maternal salivary samples to predict early mother-infant bonding problems.

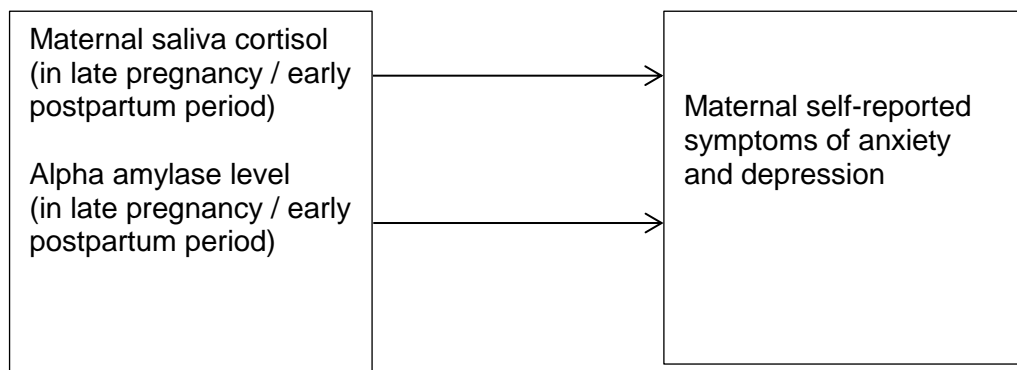
4.2.1.1 Research questions

The pilot study addressed two specific research questions:

1. *Is there a relationship between maternal saliva cortisol or alpha amylase levels in the late pregnancy or early postpartum period and impaired mother-to-infant bonding at six weeks postpartum?*



2. *Is there a relationship between maternal saliva cortisol or alpha amylase levels in the late pregnancy or early postpartum period with maternal self-reported symptoms of anxiety and depression?*



4.3 Methods

4.3.1.1 Recruitment

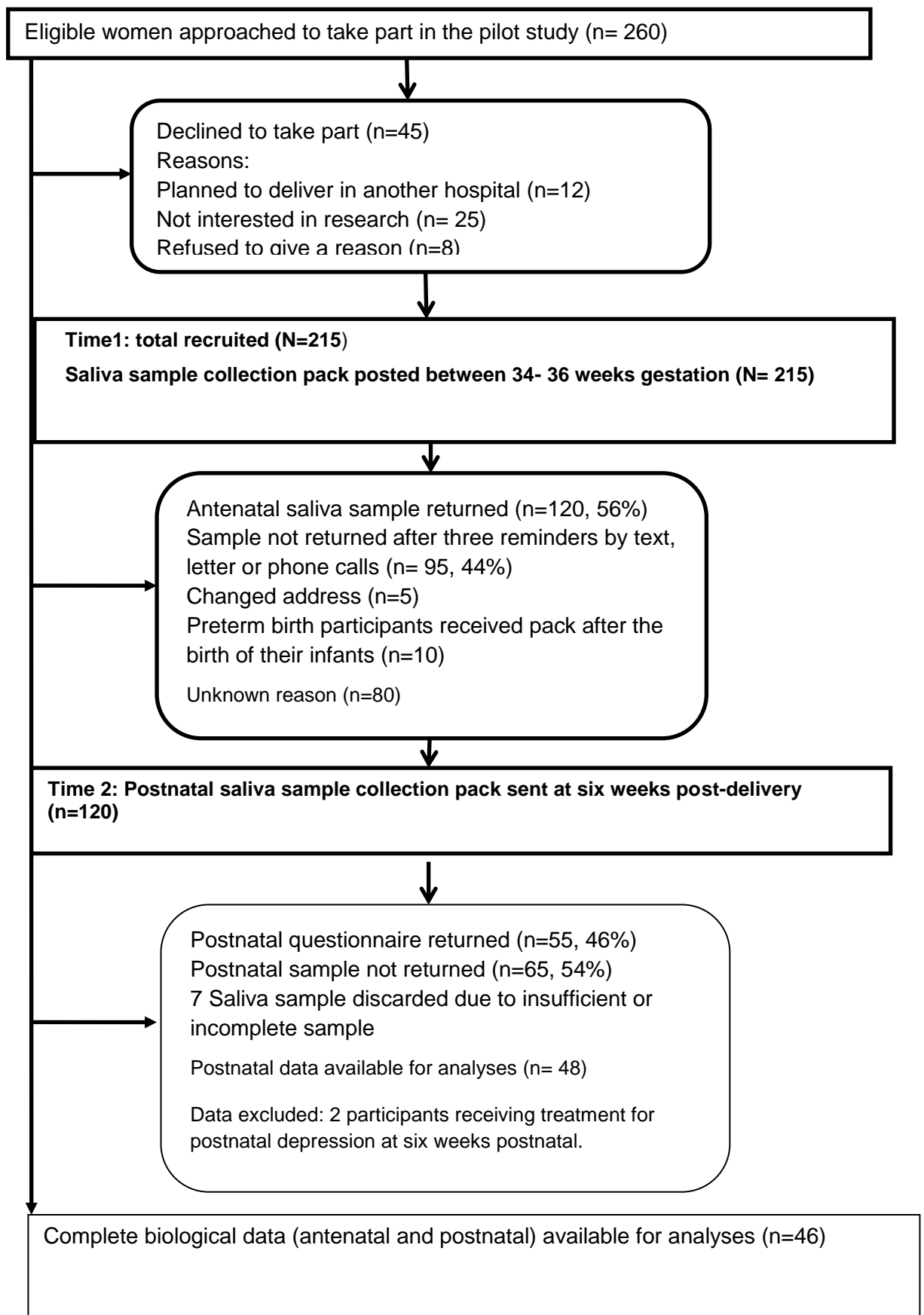
Recruitment for the pilot study commenced alongside the main study recruitment over a two-year period between 2008-2010. However, recruitment for the main study continued over a four-year period from 2008 until 2012. Each woman recruited in the main study was approached about the cortisol and alpha-amylase component of the pilot study, and offered the option of taking part in both the questionnaire and the pilot study (biological data) or just the former. Participants who agreed to take part in the pilot study were asked to complete a study consent form as well as making a tick on the questionnaire box to indicate informed consent. They were also asked to indicate their participation by making another tick in the saliva sample box (see appendix 14). To maintain confidentiality, the same unique reference number was issued to participants taking part in both studies. The women were provided with clear verbal and written instructions (see appendix 23) on how to collect the saliva sample themselves.

4.3.1.2 Flow of participants through the study and response rate

The flow of study participants through the study for the pilot study is presented in Figure 4.1 (below). In total, 215 eligible women were recruited for the pilot study. Saliva sample collection kits were sent to all of these women between 34-36 weeks gestation to be collected at 36 weeks gestation. A total of 120 women (56%) provided a saliva sample for at least one day at 36 weeks gestation; whereas 95 (44%) did not. Of the 120 women who provided

antenatal saliva samples, 55 (46%) of these also provided saliva samples at 6 weeks postnatal; whereas 65 (54%) did not return their postnatal samples. After further data exclusion, data from 46 complete cases remained for analysis (21% response rate overall).

Figure 4-1 Flow of participants through the pilot study



4.3.1.3 Biological data collection

Participants who agreed to take part in the biological data collection were sent a saliva sampling pack along with the questionnaire pack. This contained 16 saliva sampling tubes/Salivettes (Starsteadt, Germany), an information sheet and a sampling time record form (see appendix 23 and 24). The completed packs were returned to the researcher in pre-paid envelopes. As explained above, cortisol and alpha amylase have strong diurnal patterns, so data collection was required on multiple occasions throughout the day in order to capture this variation.

A total of sixteen saliva samples were collected at home per individual. It meant that samples were collected four times a day on two consecutive days during the antenatal and postnatal periods (on waking, 30 minutes later, as well as eight and 12 hours after waking). Each participant would put a sterile cotton wool roll onto their tongue and allow it to absorb the saliva in their mouth for one minute. The cotton wool roll was then placed in the Salivette tube, sealed and stored in a plastic bag with the participant number, and posted back to the researcher. As stated above, the saliva samples were checked for quantity and quality and stored at -20C until the day of assay.

4.4 Biological measures

4.4.1.1 Cortisol and alpha amylase as stress biomarkers

The two main systems comprising the psychobiology of stress are the hypothalamic-pituitary-adrenal (HPA axis) and the locus coeruleus /autonomic (sympathetic) nervous system (SNS),(Granger et al., 2007). Cortisol is routinely used to measure the function of the HPA axis, while salivary alpha amylase has been proposed as a measure of sympathetic activation (Entringer et al., 2009, Harville et al., 2009, Rothenberger et al., 2010). Maternal saliva samples were measured at 36 weeks pregnancy and again six weeks postnatal to assess the concentrations of cortisol and alpha amylase (see the data collection and management section).

4.4.1.2 Measurement of maternal cortisol and alpha amylase

The diurnal profiles of salivary cortisol and salivary α -amylase were measured using standard commercial assay kits (supplied by SalimetricsTM, PA, USA) at each time point (36 weeks gestation and six weeks postnatal). Cortisol exhibits a distinct diurnal profile; levels rise from the moment of awakening until a peak is reached 30 minutes later (the 'cortisol awakening response'), followed by declining levels throughout the rest of the day (Pruessner et al., 1997). Whereas, salivary alpha amylase shows a distinct diurnal pattern that is opposite to cortisol with a post awakening decrease followed by an increase throughout the afternoon into the evening (Rohleder et al., 2004, van Stegeren et al., 2008).

4.5 Saliva sample assay preparation

Once received, the samples were centrifuged at 3,000g for 15 minutes at 4°C in order to extract saliva from the Salivettes. Additionally, the samples were checked for incorrect labelling, as well as any signs of contamination and a record was made of any contaminated samples. The Salivettes were then discarded, and the samples frozen at -20°C until required for assaying.

4.5.1.1 Principles of salivary cortisol assay

A competitive enzyme immunoassay was used for the quantitative measurement of salivary cortisol. Cortisol in the saliva samples and in standards competes with that linked to horseradish peroxidase for antibody binding sites on the surface of microtitre plate wells. Following incubation, any unbound components are washed away, allowing bound cortisol peroxidase to be measured via its reaction with the substrate tetramethylbenzidine (TMB), which results in a blue colour change. After another incubation period, sulphuric acid is used to stop the reaction, giving rise to a yellow colour change. Finally, the optical density (OD) of cortisol peroxidase is read on a plate reader at 450nm. The OD of cortisol peroxidase is inversely proportional to the amount of cortisol present. A cortisol standard curve generated from the ODs of the cortisol standards is used to determine the concentration of salivary cortisol in the samples (Khalife, 2009), unpublished thesis.

4.5.1.2 Principles of salivary α -amylase assay

A kinetic enzyme assay was used to measure α -amylase activity, which reflects α -amylase levels. This technique involves the enzymatic action of α -amylase on a chromagenic substrate, 2-chloro-p-nitrophenol linked with maltotriose, to yield 2-chloro-p-nitrophenol, resulting in a yellow colour change, which can be spectrophotometrically measured at 405 nm. OD readings are obtained at one minute and three minutes, and the change in absorbance over this time is used to calculate the units of amylase (units/ml) present in the sample (Khalife, 2009), unpublished thesis.

4.6 Data analysis of pilot study

4.6.1.1 Analysis to address pilot study research question 1:

Is there a relationship between maternal saliva cortisol or alpha-amylase levels in late pregnancy or during the early postpartum period and poor mother-infant bonding 6 weeks postpartum?

Prior to performing any statistical analyses on the biological data, the data were manually entered into SPSS (version 20.0 for Windows), and assessed for normality of distributions using P-P plots. The cortisol and α -amylase data exhibited a skewed distribution. To reduce skewness, the data was natural log (Ln) transformed in an attempt to normalise the distribution. Following the log transformations, all data appeared normally distributed meaning that parametric statistical tests were appropriate and could be used to analyse the biochemical data. As a normal distribution could not be established with the mother to infant

bonding data even after log transformations, non-parametric statistics were used for all data analysis involving mother-infant bonding score.

Non-parametric Spearman's rank order correlation analysis was used to determine if there was an association between values of maternal salivary cortisol and alpha amylase collected during the Time 1 (antenatal) and Time 2 (postnatal) periods with the scores obtained from the mother-to-infant bonding questionnaire, at first week and 6 weeks postnatal.

CHAPTER 5 RESULTS

As described in the previous chapter, data from participants in the main study group, including psychometric data, were obtained from self-completed questionnaires, while the women recruited to the pilot study provided biological and psychometric data. For clarity, the main study and pilot study results are presented in this chapter in the following sections.

Section one presents the study response rate, sample characteristics, and descriptive statistics for the psychometric measures from the survey data collected at Time 1 (antenatal) and Time 2 (1 week and 6 weeks postnatal). Section two presents the chi-square and logistic regression results from the cohort survey to answer the following research questions:

- 1. Does depression or other psychological problems in late pregnancy predict poor mother-to infant bonding at six weeks postnatal?*
- 2. Do psychometric measures of postnatal anxiety or depression correlate with the Mother to Infant Bonding Scale?*

Section three presents the outcomes of the comparison of data from women with high or low risk pregnancies, which addresses the third research question:

- 3. Does having a high obstetric risk pregnancy affect mother-infant bonding?*

Section four presents the results of the cortisol biomarker subsample, to explore research questions four and five.

4. *Is there a relationship between maternal saliva cortisol or alpha amylase levels in the late pregnancy or early postpartum period and impaired mother-to-infant bonding early weeks postpartum?*
5. *Is there a relationship between maternal saliva cortisol or alpha amylase levels in the late pregnancy or early postpartum period and maternal self-reported symptoms of anxiety and depression?*

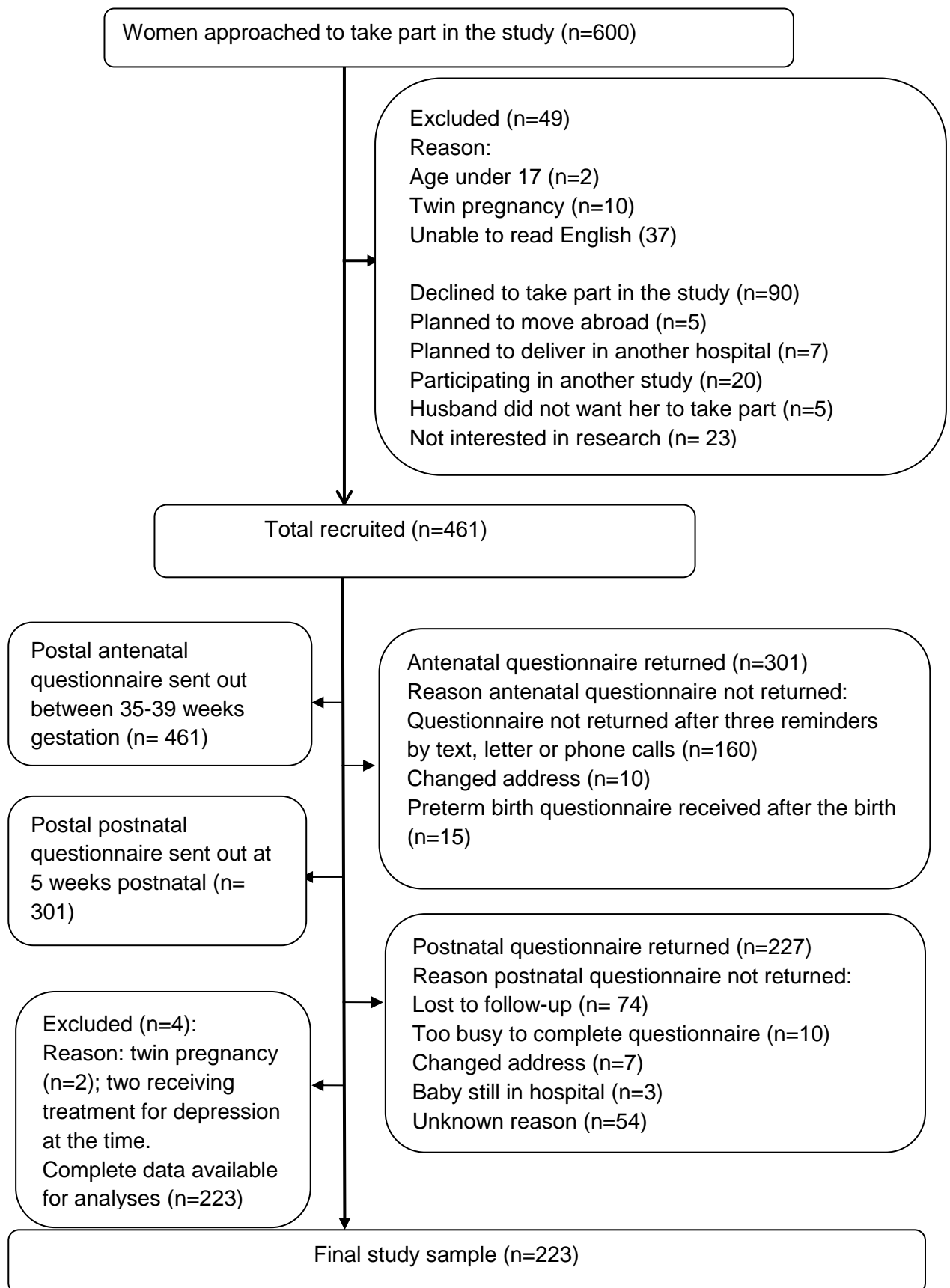
5.1 Section One: Cohort Study Response Rates, Sample Characteristics and Descriptive Statistics

5.1.1.1 Recruitment and response rate

A total of 600 eligible women were approached to take part in this cohort study between 2008 and 2012. Figure 5.1 summarises participant recruitment. Of the 461 eligible women initially recruited, 160 (35%) did not return the antenatal questionnaire (after three reminders) and were excluded from the study (referred to as antenatal non-respondents); 301 women (65%) returned the antenatal questionnaire. Of these, 227 women (75%) returned the postnatal questionnaires. The 77 (25%) who did not return the postnatal questionnaire are referred to as postnatal non-respondents.

Four women were excluded (two during the antenatal and two during the postnatal period) in line with study exclusion criteria, as two had twin pregnancy; and two women were receiving treatment for severe depression at the time. This resulted in a final study sample size of 49% (n=223); referred to as study respondents.

Figure 5-1 Flow of participants through main study



5.1.1.2 Comparison of respondents versus non-respondents

In cohort studies, particularly those based on postal questionnaires, non-response is a potential problem. The results of a study can be biased if there are systematic statistically significant differences between the non-respondents and respondents. If the groups differ significantly, then the results are not representative for the entire population (Landsmeer-Beker et al., 2006).

Non-response bias was assessed statistically using a Chi-square test for independence. The baseline socio-demographic and obstetric data, obtained from the women on recruitment were compared between respondents and non-respondents at both Time 1 (36 weeks antenatal) and Time 2 (6 weeks postnatal) (Table 5.1). Variables compared included: maternal age at recruitment, gestation of pregnancy at recruitment, parity, history of miscarriage, maternal ethnicity, marital status, highest educational qualification, maternal occupation, smoking and alcohol consumption in pregnancy. These variables were considered to be potential confounders for the main variable (mother-to-infant bonding) (Figueiredo et al., 2009, Bicking Kinsey and Hupcey, 2013).

Statistically significant differences between respondents and non-respondents were found for six factors, including gestational age at recruitment, which was significantly higher among Time 2 non-respondents than respondents ($p=.01$), education, as women with a degree, masters, or PhD were significantly more likely to complete both the antenatal and postnatal questionnaires ($p=.04$); non-respondents were less likely to be in professional/managerial classes ($p=.02$),

women who were single and not living with their partners had a lower response rate at both times compared with women who were married or living with partners ($p<0.001$), nulliparous women had a higher response rate ($n = 184$, 82%) than multiparous women ($n = 40$, 18%), ($p=.01$), and smoking status; non-smoker, ($n=222$ (99%); smoking in pregnancy ($n=2$, 1%), $p<0.02$). Respondents and non-respondents did not differ significantly in maternal age, ethnicity, being born in the UK, or alcohol intake during pregnancy or miscarriage.

Table 5-1 Socio-demographic and obstetric characteristics of study respondents and non-respondents

Socio-demographic variables	All 461	Non-Respondents		Respondents Study Sample Antenatal & postnatal 223 (48%)	Difference p-value
		Time 1 (Antenatal) 160 (35%)	Time 2 (Postnatal) 77 (17%)		
Gestational age at recruitment	M: 29.61 ±5.632 R: 17 to 41	M: 28.44 ±5.730 R: 17 to 41	M: 31.43 ±5.641 R: 17 to 41	M: 29.82 ±5.386 R: 17 to 4	0.01
Maternal age	M: 31.98 ±5.199 R: 17 to 44	M: 31.46 ±5.295 R: 17 to 44	M:31.35 ± 5.360 R:17- 43	M: 32.57 ± 5.030 R: 18 to 44	0.06
Age groups					0.65
17-24	40 (9%)	16 (10%)	8 (10%)	16 (7%)	
25-30	126 (27%)	46 (29%)	22 (29%)	58 (26%)	
31-35	179 (39%)	64 (40%)	30 (39%)	85 (38%)	
36-44	116 (25%)	34 (21%)	17 (22%)	65 (29%)	
Ethnicity					0.50
White	301(65%)	102 (64%)	46 (60%)	153 (68%)	
Mixed	26 (6%)	10 (6%)	2 (3%)	14 (6%)	
Asian	59 (13%)	22 (14%)	14 (18%)	23 (11%)	
Black	39 (9%)	16 (10%)	7 (9%)	16 (7%)	
Other	36 (8%)	10 (6%)	8 (10%)	18 (8%)	
Born in UK	260 (56%)	88 (55%)	42 (55%)	130 (58%)	0.79
Outside UK	201 (44%)	72 (45%)	35 (46%)	94 (42%)	
Education					
O'Levels/GCSEs	62 (13%)	28 (18%)	14 (18%)	20 (9%)	

Socio-demographic variables		Non-Respondents		Respondents	Difference p-value
	All 461	Time 1 (Antenatal) 160 (35%)	Time 2 (Postnatal) 77 (17%)	Study Sample Antenatal & postnatal 223 (48%)	
A levels/ vocational training	43 (9%)	15 (9%)	11 (14%)	17 (8%)	0.04
Degree/masters /PhD	356 (77%)	117 (73%)	52 (68%)	187 (83%)	
Marital status					0.01
Married	300 (65%)	94 (59%)	46 (60%)	160 (71%)	
Living with partner	109 (24%)	42 (26%)	15 (20%)	52 (24%)	
Alone	52 (11%)	24 (15%)	16 (20%)	12 (5%)	
Occupation					0.02
Professional	192 (42%)	70 (44%)	22 (29%)	100 (45%)	
Managerial	101(23%)	37 (23%)	15 (19%)	49 (22%)	
Skilled/unskilled	83 (17%)	32 (20%)	15 (19%)	36 (16%)	
Others	85 (18%)	21 (13%)	25 (33%)	39 (17%)	0.01
Parity					
Nulliparity	377 (82%)	148 (93%)	45 (58%)	184 (82%)	
Multiparty	84 (18%)	12 (7%)	32 (42%)	40 (18%)	0.09
Miscarriage					
No	358 (78%)	132 (82%)	54 (70%)	172 (77%)	
Yes	103 (22%)	28 (18%)	23 (30%)	52 (23%)	0.11
Alcohol in take					
No	407(88%)	144 (90%)	72 (94%)	191(85%)	
Yes	54 (12%)	16 (10%)	5 (6%)	33 (15%)	

Socio-demographic variables		Non-Respondents		Respondents	Difference p-value
	All 461	Time 1 (Antenatal) 160 (35%)	Time 2 (Postnatal) 77 (17%)	Study Sample Antenatal & postnatal 223 (48%)	
Smoking status					0.02
Non-smoker	456 (99%)	160 (100%)	74(96%)	222 (99%)	
Smoking in pregnancy	5 (15)	0 (0%)	3 (4%)	2 (1%)	
Note: GCSE, General Certificate of Secondary Education (age 16); A-level, Advanced Level Examinations (age 18). Data are shown as mean, (\pm SD), (R=range) number (n), percentage (%) where appropriate.					

5.2 Socio-demographic characteristics

The mean age of the study participants ($n=223$) who completed both antenatal and postnatal questionnaires was 33 years (SD 5.0), range 18 to 44 years. The average gestation of pregnancy at which the women were recruited was 30 weeks ($SD = 5.4$, range: 17 to 41 weeks). White women formed the largest ethnic group, within the study sample 153 (68%), followed by Asian women (23, 11%) and African, Black Caribbean or women of Black British origin (16, 7%). Over half of the participants were born in the United Kingdom (UK), 130 (58%).

In terms of education, over one-third of the respondents had attended higher education, with 97(44%) educated to masters or PhD level, and 90 (40 %) to under-graduate degree level. Smaller proportions of women had completed their education at A levels/vocational training or equivalent ($n = 17$, 8%) or O level/GCSE or equivalent ($n = 20$, 9%). In terms of occupation, a high proportion of participants classed their jobs as professional ($n = 100$, 45%) or managerial, 49 (22%). Other occupations were classed as skilled or unskilled, 36 (15%), whereas students and housewives were combined in the same category and totalled 39 (17%).

71% of participants ($n = 160$) were married, 52 (23%) were living with a partner, and 12 (5%) were recorded as single and not living with a partner; 33 participants reported drinking alcohol in pregnancy (16%). Only two participants (1%) reported smoking in pregnancy.

5.2.1.1 Obstetric characteristics and pregnancy risk factors

The majority of participants (82%, n=184) were nulliparous (first time mothers), with 40 participants (18%) having their second or higher birth order baby. All participants were asked if they had ever experienced a miscarriage. Around three quarters, 172 (77%) had not, with 23% (n=52) of women experiencing one or more miscarriage before this pregnancy. Most participants were not on medication (n = 171/76%), and those who were had been prescribed medication for a medical problem in pregnancy (n = 53/24%), for example, anti-hypertensive, anti-diabetics or obstetric cholestasis drugs.

5.2.1.1.1 High and low risk pregnancy

Women were classified into two groups, high (n=66/30%) or low risk pregnancy (n=157/70%). Table 5.2 summarises the obstetric characteristics of both groups. Women were classed as having a 'high risk pregnancy' if they had one or more pre-pregnancy health or obstetric problems (pre-existing or onset during pregnancy), which required additional care in pregnancy using criteria based on antenatal guideline from the National Institute for Health and Care Excellence (NICE, 2008b).

High risk women were further categorised for study purposes as having (1) a pre-existing medical problem (e.g. asthma, polycystic ovarian syndrome, multiple sclerosis, hypothyroidism and hyperthyroidism), (n=28/42%), and (2) disorders with an onset triggered specifically by pregnancy (e.g. gestational diabetes, obstetric cholestasis, pre-eclampsia, hypertension and hyperemesis,

placenta Previa, pre-term labour, deep venous thrombosis and anaemia), (n=38/58%), (see Table 5.2).

Table 5-2 High and low risk pregnancy groups

Obstetric characteristics	Frequency (%)
High risk pregnancy	66 (30%)
Low risk pregnancy	157 (70%)
Pre-existing medical conditions	28 (42%)
Asthma, polycystic ovarian syndrome, multiple sclerosis, hypothyroidism, hyperthyroidism and any other medical problems.	
Conditions diagnosed in pregnancy	38 (58%)
Obstetric cholestasis, pre-eclampsia, hypertension, gestational diabetes, hyperemesis, placenta previa, vaginal bleed and deep vein thrombosis.	

5.2.2 Labour and birth outcomes

Table 5.3 shows the labour and birth outcomes of interest. These included mode of birth, pain relief in labour and birth complications (in the woman and/or her infant) up to 24 hours postnatally. Ninety-six (43%) women had a spontaneous vaginal delivery; and 48 (21%) an instrumental birth (ventous extraction or forceps delivery). Over one-third of women had a caesarean section (n= 79/36%), of which 44 (20%) had a planned caesarean and 35 (16%) had an emergency caesarean.

Epidural was the most frequently used method of pain relief by 68% of the participants (n=154), followed by entonox, commonly known as gas and air (n=48/22%), and a minority of participants (n=6, 3%) had only pethidine. Fifteen (7%) of the women had no pain relief in labour.

Complications at birth were classified into two categories due to their small number. Fifty one women (23%) had complications which included postpartum haemorrhage (defined as estimated blood loss >1000mls), or severe perineal tear (3rd or 4th degree) repaired in theatre.

Table 5-3 Labour and birth outcomes

Labour and birth outcome variables	Number (%) N=223
Duration of labour (in hours)	Mean: 8.52 SD: 4.844 Range: 1-27
Mode of birth	
Spontaneous delivery	96 (43%)
Instrumental delivery	48 (21%)
Elective caesarean section	44 (20%)
Emergency caesarean section	35 (16%)
Labour pain relief	
No pain relief	15 (7%)
Pethidine	6 (3%)
Entonox inhalation	48 (22%)
Epidural	154 (68%)
Maternal and neonatal complication	
No	173 (77%)
Yes	51 (23%)

5.2.3 Neonatal outcomes

Neonatal outcomes of interest included gestational age at birth, infant gender, birth weight, head circumference and Apgar score at one and five minutes. The average gestational age was 39 weeks (range 32-42). Most babies were born at term ($n = 217/97\%$), with a small number born preterm ($n = 7/3\%$). Mean infant birth weight was 3,360gm (1520-5162gm), and mean infant head circumference 35cm (range: 28-39cm). Apgar scores at one minute ranged from 4 to 10 (mean = 8), while scores at five minutes ranged from 7 to 10 (mean = 9). There were a similar number of boys ($n = 111/50\%$) and girls ($n = 113/50\%$) born to this cohort.

5.2.4 Infant feeding

Based on obstetric records, 89% ($n = 199$) of women breastfed their babies at birth. When they were asked how they fed their infants at six weeks postnatal, 67% ($n = 149$) reported exclusively breastfeeding, 22% ($n=50$) combined bottle and breast feeding (mixed feeding), whilst 11% ($n = 25$) exclusively bottle-fed. Of the 199 women who either breastfed exclusively or implemented mixed feeding, when asked at six weeks postnatal, 48% ($n = 96$) of these did so within one hour of giving birth, 26% ($n = 51$) within one to four hours, and 17% ($n = 34$) between five and 24 hours post-birth. Twenty eight women (14%) did not respond to the question on infant feeding initiation.

5.3 Antenatal psychometric measures

Five psychometric tools were used to measure the antenatal psychosocial factors in late pregnancy. Table 5.4 shows descriptive statistics (mean, standard deviation and range) for these measures. The majority of data were normally distributed; however the MAAS and SLES scales had a skewed distribution.

Table 5-4 Antenatal psychometric measures

Antenatal psychometric measures	N	Mean	SD	Obtained Range		Possible range
				Min	Max	
MAAS	219	79.7	7.24	57	95	19-95
Antenatal STAI-State	223	35.6	10.15	20	75	20-80
Antenatal STAI-Trait	223	35.4	8.66	20	59	20-80
Antenatal EPDS	223	6.5	4.27	0	21	0-30
Antenatal SLES	223	2.1	2.86	0	16	0-52
Antenatal SAPAS	223	1.7	1.40	0	6	0-8
Abbreviations: MAAS= Maternal Antenatal Attachment Scale; STAI= Spielberger State Anxiety Inventory; EPDS= Edinburgh Postnatal Depressive Scale; SLES= Stressful Life Events Scale; SAPA= Standardised Assessment of Personality Abbreviated Scale						

5.3.1 Edinburgh Postnatal Depression Scale

To screen for risk of depression during pregnancy, participants (N=223) completed the EPDS questionnaire between 36 to 40 weeks pregnant. The mean depression score was 6.5 ($SD = 4.27$, range= 0-21). Risk of depression was defined as an EPDS score ≥ 13 ; 23 (10%) women scored 13 or higher on the scale, indicating just over 10% of women were at risk of depression.

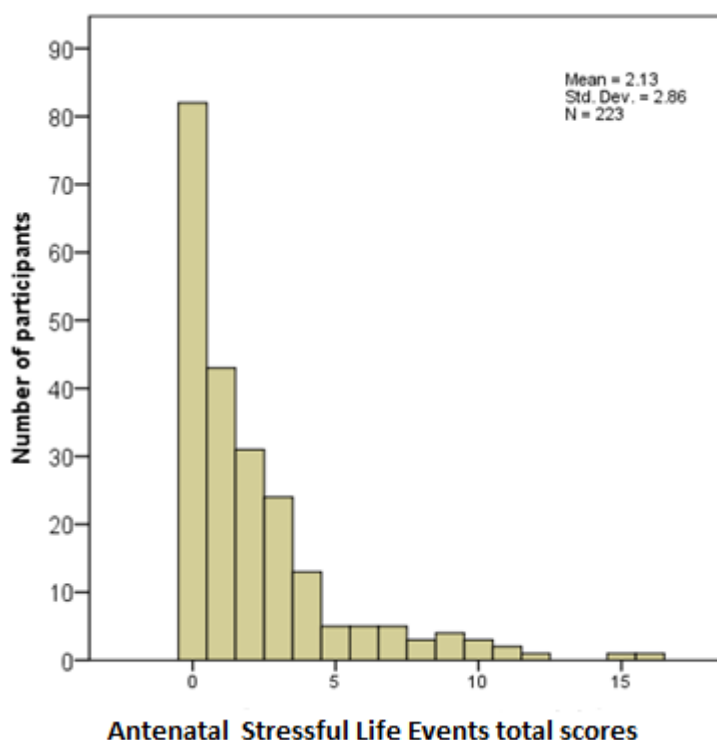
5.3.2 Spielberger State and Trait Anxiety Scale

Maternal antenatal anxiety was measured using the Spielberger State and Trait Anxiety inventory (STAI). Mean state anxiety was 36.2 ($SD = 10.46$; range: 20-75); and mean trait anxiety was 35.5 ($SD = 8.83$; range: 20-59). A score of ≥ 40 on the Spielberger State-Trait scale is considered indicative of high anxiety (Grant et al., 2008). Using this criterion, 101 (34%) women had a score of ≥ 40 indicating high state anxiety; and 88 (29%) had high trait anxiety.

5.3.3 Stressful Life Events Scale (SLES)

Maternal antenatal stress was measured using the SLES. The distribution of SLES scores is illustrated in Figure 5.2. As can be seen, the life events scores showed a highly positively skewed distribution indicating most women had a low level of stressful life events when assessed antenatally. However, 30 (14%) of women in the cohort had five or more stressful life events during pregnancy.

Figure 5-2 Distributions of antenatal SLES scores in the study cohort



5.3.4 Standardised Assessment of Personality Abbreviated Scale (SAPAS).

Maternal personality disorder was assessed using the Standardised Assessment of Personality Abbreviated Scale (Moran et al., 2003). The mean score was 1.7 ($SD=1.4$; range: 0-6.). 224 (75%) women had no personality disorder with a score of ≤ 3 , while 76 (25%) had a probable personality disorder having recorded a higher score.

5.3.5 Maternal Antenatal Attachment Scale (MAAS)

Maternal fetal bonding was assessed using the Maternal Antenatal Attachment Scale (MAAS, Condon, 1993). Mean total attachment was 79.8 ($SD = 7.3$; range: 57 to 95), mean 'Quality of attachment' was 46.2 ($SD = 3.3$; range = 32

to 50); and mean 'Time spent on attachment' was 29.4 ($SD = 4.4$; range = 18 to 40). A score of ≥ 76 on the total attachment score has been used as cut-off to determine high and low fetal attachment (Pollock and Percy, 1999, Hart and McMahon, 2006). Using same criteria, 68 (23%) of women in the current study had poor fetal bonding while 228 (77%) had good fetal bonding.

5.4 Postnatal psychometric measures

5.4.1 Mother-to- Infant Bonding Scale (MIBS)

The distribution of MIBS scores among women at the first week postnatal and six weeks postnatal are presented in figures 5.3 and 5.4. The scores for both times showed a highly positively skewed distribution, with scores concentrated to the left of the mean, indicating that most women bonded well with their infants. The MIBS score was treated as a binary variable to distinguish women who had "good bonding" with their infants, (total score ≤ 2) and those with "poor bonding" (total score ≥ 2). 83 women (38%) had a score of 2 or more during the first week of birth and 46 (21%) at 6 weeks postnatal. As data were skewed, a non-parametric Wilcoxon Signed Ranks test was used to compare MBIS scores at 1 week and 6 weeks postnatal, which showed that the mother-to-infant bonding score improved significantly between the first week of birth and 6 weeks postnatal, ($z = -7.74$, $p < 0.001$).

The term "Good and poor bonding score" illustrates how the scores were used in the original studies, it is not a value judgement within this thesis.

Figure 5-3 Distribution of MIBS first week scores in the study cohort

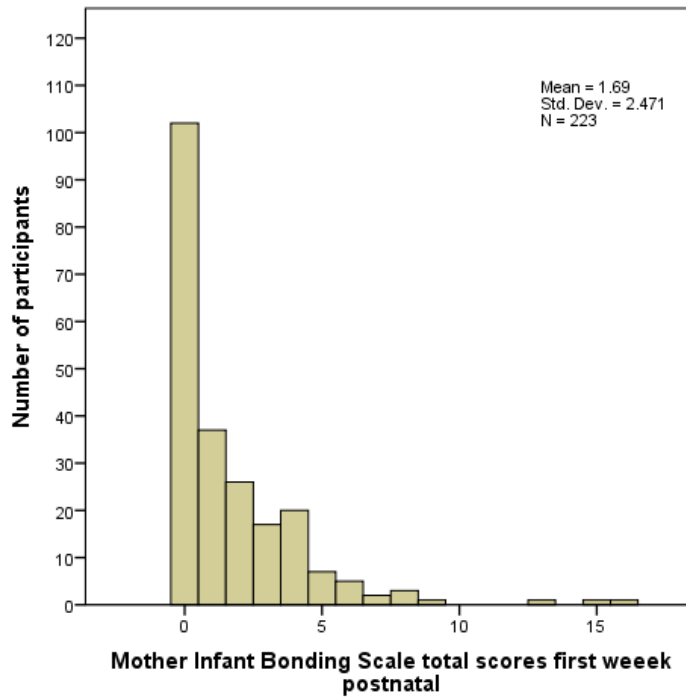
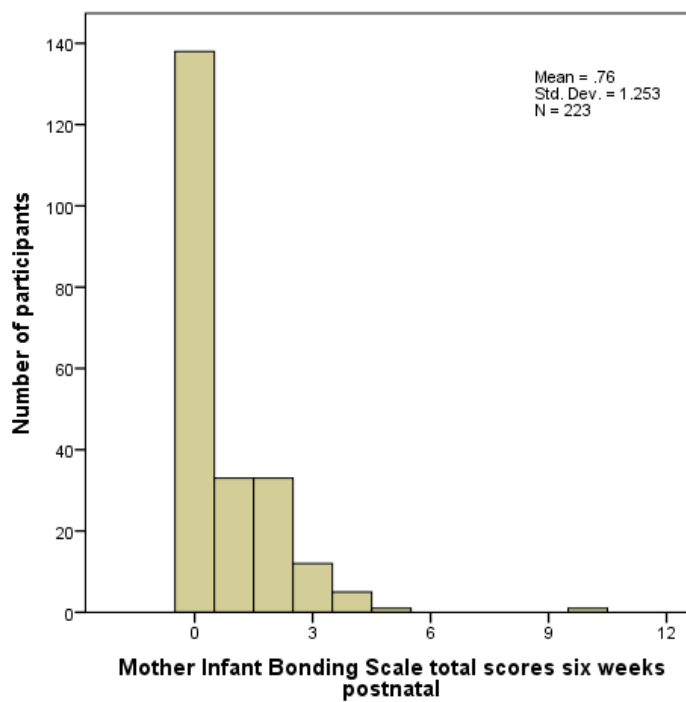


Figure 5-4 Distribution of MIBS six weeks scores in the study cohort



5.4.2 Postnatal Edinburgh Postnatal Depression Scale

The EPDS was completed by 223 women at six weeks postnatally. The average score was 7.00 ($SD = 4.6$, range: 0 - 22). Twenty six women scored 13 or above indicating postnatal prevalence rate of risk of depression of 12%. There was a statistically significant correlation between participants' antenatal and postnatal EPDS scores. The postnatal EPDS mean was slightly, but not significantly higher than the antenatal one (mean difference = -0.47, $SD = 4.23$, 95%CI = -1.02 to 0.97, $t = -1.63$, ns) indicating that women who were depressed antenatally may continue to be depressed postnatally.

5.4.3 Postnatal Spielberger State & Trait Anxiety Inventory (STAI)

Maternal postnatal anxiety was measured using the Spielberger State and Trait Anxiety Inventory (STAI) questionnaire (Spielberger et al., 1983). The mean State score was 33 (range = 20 - 73; $SD = 10.1$; $n = 223$), whilst the mean Trait score was 34 (range = 20 - 67; $SD = 9.0$; $n = 223$). The incidence of postnatal anxiety was estimated using a cut off of 40; 52 (23%) women had a score of 40 or higher for State anxiety, whilst for Trait anxiety this figure was 62 (29%).

There was a statistically significant correlation between the antenatal and postnatal State ($r = 0.49$, $p < 0.001$, $n = 223$) and Trait scores ($r = 0.62$, $p < 0.001$, $n = 223$). Moreover, the results showed a statistically significant difference between the antenatal and postnatal State mean score (mean difference = 2.5, $SD = 10.2$, 95%CI = 1.2 to 3.8, $t = 3.67$, $p < 0.001$) and the Trait mean score (M

= 1.1, $SD = 7.7$, 95%CI = 0.09 to 2.12, $t = 2.14$, $p < 0.03$). Overall, there was a reduction in maternal anxiety during the antenatal to postnatal period.

5.4.4 Stressful Life Events Scale (SLES)

Maternal postnatal stress was measured using the Stressful Life Events Scale (Bergman et al., 2007). Similar to the antenatal life events, the distribution of the postnatal life events scores was highly skewed indicating that most women in the current study had few stressful events as measured using this measure. The mean score was 2 ($SD = 2.6$, range 0 - 16). There were no statistically significant differences between the antenatal and postnatal scores ($M = 0.02$, $SD = 2.8$, 95%CI = -0.34 to 0.39, $t = 0.12$).

5.4.5 Standardised Assessment of Personality Abbreviated Scale (SAPAS).

Maternal personality trait was assessed postnatally using the SAPAS (Moran et al., 2003). The mean postnatal score was 1.7 ($SD = 2.67$, range = 0 - 6), similar to the antenatal score.

5.4.6 Summary

This section has presented the antenatal and postnatal questionnaire response rates, socio-demographic characteristics of study participants, and comparison of respondents and non-respondents. Overall, baseline characteristics were comparable in most of the socio-demographic variables of interest. Descriptive

statistics for the antenatal and postnatal psychological outcome measures were also presented. The next section addresses the relationship between these variables and the primary research outcome, namely, mother-infant bonding.

5.5 Section Two: Mother-Infant Bonding Outcomes

This section presents results relevant to answer the primary research question namely if maternal anxiety, stress, depression and poor maternal fetal bonding during late pregnancy (circa 36 weeks antenatal) predicted mother-to-infant bonding problems at six weeks postnatal.

5.5.1 Socio-demographic characteristics and mother-infant bonding

Women's socio-demographic characteristics considered to be potential confounders for poor mother-infant bonding include: age, marital status (living alone or not), ethnicity, education and occupation. Relationships between study variables and potential confounders were examined using Chi-square tests for independence for categorical or binary variables, and independent sample t-tests were used for continuous variables. The results showed no statistically significant associations between any socio-demographic characteristics of interest and mother-to-infant bonding scores at six weeks postpartum (table 5.5).

Table 5-5 Socio-demographic characteristics and study outcome

Socio-demographic		Mother-infant bonding scores 6 weeks			X ² P-value /t-test
		Total sample N=223	Good bonding N=177 (80%)	Poor bonding N= 46 (20%)	
Age in years			Mean, 33 SD, 5.0	Mean, 32 SD,5.0	0.40
Age groups					0.97
	17-24	15	12 (80%)	3 (20%)	
	25-30	59	46 (78%)	13 (22%)	
	31-35	85	68 (79%)	18(21%)	
	36-44	64	53 (81%)	12(19%)	
Ethnicity					0.98
	White	151	119(79%)	32(21%)	
	Mixed	14	12(86%)	2(14%)	
	Asian	23	18(78%)	5(22%)	
	Black	16	13(81%)	3(19%)	
	Other	18	14(78%)	4(22%)	
Born in UK					0.39
	Yes	128	104(81%)	24(19%)	
	No	95	73(77%)	22(23%)	
Education					0.90
	O'LEVELS /GCSE	19	16(84%)	3(16%)	
	A LEVELS/ vocational training	16	13(81%)	3(19%)	
	Degree	91	73(81%)	18(19%)	
	Higher degree	97	75(77%)	22 (23%)	
Occupation					0.50
	Professional	100	84(84%)	16(16%)	
	Managerial	49	37(75%)	12(25%)	
	Skilled/unskilled	35	27(78%)	8(22%)	
	Others	39	29(75%)	10(25%)	
Marital status					0.39
	Married	58	129(82%)	29(18%)	
	Living with partner	53	39(74%)	14(26%)	
	Alone	12	9(75%)	3(25%)	

Exact Sig. (2-sided) are presented as Pearson Chi-Square or Fisher's Exact Test where the number expected within a table cell is less than 5

5.5.2 Obstetric outcomes and mother-infant bonding

Pregnancy, labour and birth outcomes considered to be potential mediators of poor postnatal mother-to-infant bonding included parity, history of previous miscarriage, mode of birth, pain relief in labour and birth complications.

A chi-square test for independence was performed to explore possible associations between pregnancy, labour and birth outcomes and mother-infant bonding status. The results (Table 5.6) showed the proportion of women who scored 2 and above for maternal bonding was significantly higher in women who had epidural pain relief in labour, (27%, $n = 41$) when compared with women who did not (7%, $n = 5$). ($n = 223$, $\chi^2 = 11.0$, $p = .001$). There was no statistically significant association between mother-infant bonding and parity, mode of birth or maternal complications at birth.

Table 5-6 Labour, birth and study outcome

Obstetric characteristics		Mother-infant bonding scores 6 weeks postnatal			X ² P-value
		223	Score ≤2 N=179 (80%)	Score ≥2 N= 46 (20%)	
Parity	Nulliparity	182	145(80%)	37(20%)	0.81
	Multiparity	41	32(78%)	9(22%)	
Mode of delivery	Spontaneous	95	83(86%)	14(14%)	0.21
	Instrumental	48	38(80%)	10(20%)	
	Elective C/S	44	32(73%)	12(27%)	
	Emergency C/S	34	24(71%)	10(29%)	
Method of pain relief	No pain relief	15	14(93%)	1(7%)	0.01
	Pethidine	6	5(83%)	1(17%)	
	Entonox	48	45(94%)	3(6%)	
	Epidural	154	113(73%)	41(27%)	
Pain relief combined Epidural /no epidural	Yes	154	113(73%)	41(27%)	0.001
	No	69	64 (93%)	5(7%)	
Maternal complication at birth	Yes	50	37(74%)	13(26%)	0.29
	No	173	140 (81%)	33(19%)	

5.5.3 Neonatal outcomes and mother-to-infant bonding

Neonatal outcomes included gestational age at birth, infant birth weight, Apgar scores and infant gender. Table 5.7 shows that gestational age at birth (<37 weeks and ≥37 weeks gestation) and gender of the baby were not statistically significant. An independent-samples t- test was used to compare infant birth weight, Apgar score at 1 and 5 minutes between women with bonding scores of <2 or ≥2. There were no statistically significant differences between bonding scores at six weeks postnatal and any neonatal outcomes. Infant mean birth weight for women with bonding scores ≥2 was 3400gm (*SD* = 60) and <2 (*M* = 3394gm, *SD* = 55); *t* = -0.98, *p* = 0.9; 95%CI. There was a slight trend in better bonding with a female infant compared to a male infant (*p* = 0.06).

Table 5-7 Neonatal outcomes and study outcome

Neonatal outcomes	Mother--infant bonding 6 weeks		t-test / χ^2	95%CI		P-value
	Score <2 170 (77%)	Score ≥2 46 (21%)		lower	higher	
Birth weight in grams	M:3394gm±55	3400gm±60	-0.10	-189	177	0.98
Apgar at 1minute	M:8±1.3	9±1.0	-1.20	-0.7	0.2	0.21
Apgar at 5mins	M:10±0.6	10±0.6	-0.66	-0.3	0.1	0.50
Gestational age at birth			0.24			0.30
Preterm birth<37	5 (63%)	3 (38%)				
Term birth≥37	166 (77%)	49 (23%)				
Infants gender			3.52			0.06
Male	79 (72%)	31 (28%)				
Female	93 (81%)	21(19%)				

5.5.4 Maternal infant feeding and mother-to-infant bonding

There was no significant association between method of infant feeding and mother-infant bonding at six weeks postnatal (see table 5.8). Good and poor bonding scores were similar regardless of method of feeding. In addition, timing of breastfeeding initiation was not associated with mother-to-infant bonding score.

Table 5-8 Infant feeding and study outcome

Infant feeding six weeks postnatal		Mother-to-infant bonding 6 weeks postnatal			Pearson Chi-Square	P-value
		223	Good bonding 177 (79%)	Poor bonding 46(21%)		
Infant feeding	Breast	149	121(82%)	27(18%)	2.39	0.30
	Bottle	25	20(80%)	5(20%)		
	Mixed	49	36(71%)	14(27%)		
Breast feeding initiation		197	156(79%)	41(21%)	1.82	0.60
	0-1 hour post delivery	97	80(82%)	17(18%)		
	1- 4 hours post delivery	48	38(79%)	10(21%)		
	5- 24 hours post delivery	34	25(74%)	9(26%)		
	More than 24 hours post delivery	18	13(72%)	5(28%)		

Abbreviation: χ^2 =Chi Square; m=mean; \pm =Standard deviation

5.5.5 Antenatal psychometric outcomes and mother-infant bonding

The association between antenatal psychometric outcomes at 36 weeks gestation and mother-infant bonding score at six weeks postnatal were assessed. Any variable related to the outcome of interest with a significance level of $p < 0.05$ was treated as a potential predicting variable in subsequent analyses. A possible relationship between antenatal Spielberger State-Trait anxiety scale, EPDS, Life Events Scale, Maternal Antenatal Attachment Scale, Standardised Assessment of Personality Abbreviated Scale and Mother Infant Bonding Scale at one and six weeks post-birth was initially investigated.

There was a negative correlation between the Maternal Antenatal Attachment Scale and MIBS score at one week, ($r_s = -0.38$, $n = 217$, $p < 0.001$) and six weeks postnatal ($r_s = -0.42$, $n = 217$, $p < 0.001$). A high maternal antenatal attachment score in late pregnancy was associated with a low bonding score at one and six weeks postnatal. There was a significant correlation between the antenatal STAI, EPDS and SAPAS scores with mother-to-infant bonding at one week and at six weeks postnatal but no association between maternal antenatal stress and mother-to-infant bonding at either of these time points (table 5.9).

Table 5-9 Antenatal psychometric measures and study outcome

Antenatal psychometric measures	MIBS first week		MIBS six weeks postnatal	
	correlation coefficient	P-value	correlation coefficient	P-value
MAAS	-.38**	< 0.001	-.42**	0.001
Antenatal STAI-State	.20**	< 0.003	.29**	0.001
Antenatal STAI-Trait	.25**	< 0.001	.30**	0.001
Antenatal EPDS	.25**	< 0.001	.36**	0.001
Antenatal SLES	.04	0.522	.06	0.365
Antenatal SAPAS	.22**	0.001	.23**	0.001
<i>Data are displayed as Spearman correlation coefficients, rho (p value). Abbreviations: MIBS-mother-to-infant bonding scale, MAAS-maternal antenatal attachment scale, EPDS- Edinburgh postnatal depression scale, SAPAS- standardised assessment of personality abbreviated scale.</i>				

A Mann-Whitney U test was used to explore the difference between women with good and poor bonding score and their antenatal psychometric measures. There was a significant difference between the two groups (see table 5.10-5.11), suggesting that women with poor bonding scores at one and six weeks postnatal had higher anxiety, poor fetal bonding and a higher risk of depression during the antenatal period.

Table 5-10 Difference between women with good bonding and poor bonding scores at one week postnatal on antenatal psychometric measures

Antenatal psychometric measures	Median		Mann-Whitney U	Z	P-value
	Good bonding N=133	Poor bonding N=83			
MAAS	81.7	78.0	3081.5	-5.4	< 0.001
Antenatal STAI-State	32.0	34.0	4451.5	-2.7	0.007
Antenatal STAI-Trait	32.0	36.0	3959.5	-3.8	< 0.001
Antenatal EPDS	5.0	6.0	3961.5	-3.8	0.001
Antenatal SLES	1.0	1.0	5102.0	-1.3	0.189
Antenatal SAPAS	1.0	2.0	4355.5	-2.9	0.003
Sig. (2-tailed): P- value of <.05 is statistically significant P value of <.001 is highly significant					

Table 5-11 Difference between women with good bonding and poor bonding scores at 6 weeks postnatal on antenatal psychometric measures

Antenatal psychometric measures	Median		Mann-Whitney U	Z	p-value
	Good bonding N=171	Poor bonding N=45			
MAAS	81.0	75.0	1842.5	-5.4	< 0.001
Antenatal STAI-State	33.0	40.0	2312.0	-4.4	< 0.001
Antenatal STAI-Trait	33.0	38.0	2444.5	-4.1	< 0.001
Antenatal EPDS	5.0	9.0	2094.0	-5.0	0.001
Antenatal SLES	1.0	1.0	3308.5	-1.9	0.055
Antenatal SAPAS	1.0	2.0	2794.5	-3.3	0.001
Sig. (2-tailed): P- value of <.05 is statistically significant P value of <.001 is highly significant					

Boxplots were used to illustrate the distribution of MAAS, EPDS and STAI State-Trait anxiety scores between women with good and poor bonding scores at one (appendix 35-38) and six weeks postnatal (figure 5.5 and 5.8). The median score of MAAS was lower in women with poor mother-infant bonding, indicating poor fetal bonding in late pregnancy within that group. With regards to maternal depressive symptoms and anxiety, women who had a poor mother-infant bonding score at one and six weeks postnatal also had a higher median EPDS score and a higher Spielberger State-Trait median score in late pregnancy, indicating higher depressive and anxiety symptoms during pregnancy compared to women with good bonding scores.

Figure 5-5 Boxplots of MAAS total scores (good versus poor bonding) at 6 weeks postnatal

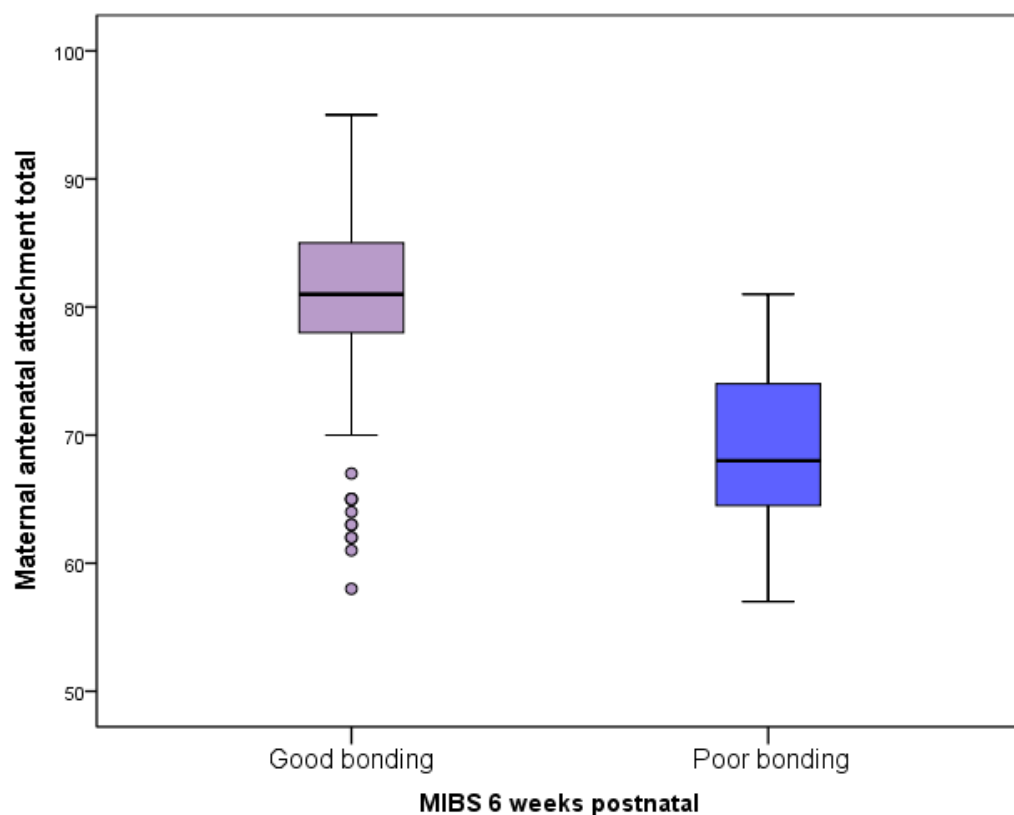


Figure 5-6: Boxplots of antenatal EPDS total scores (good versus poor bonding) at 6 weeks postnatal.

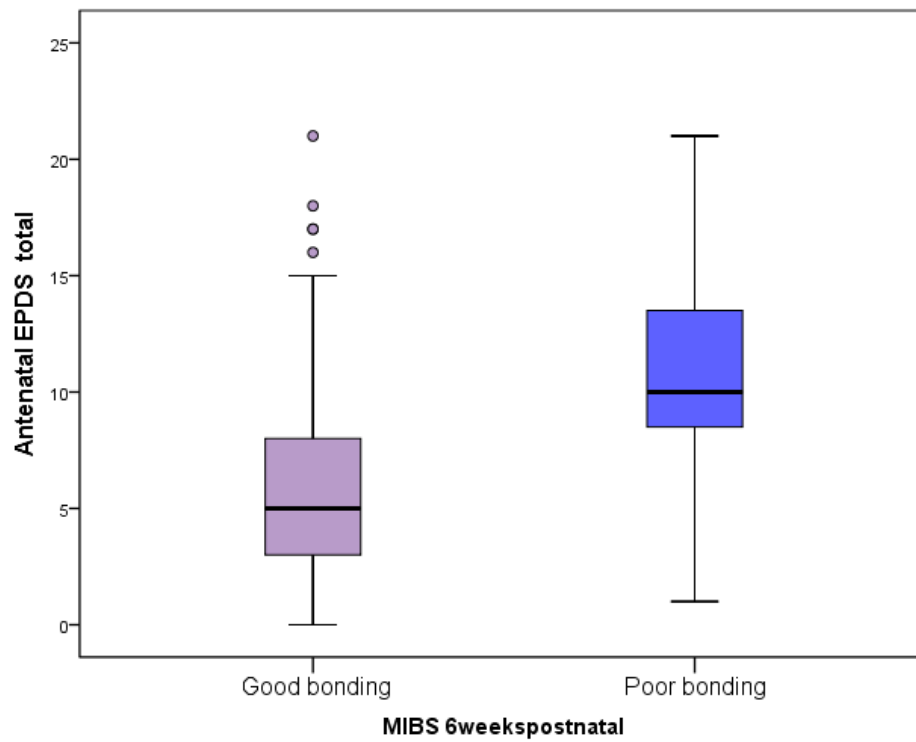


Figure 5-7 Boxplots of antenatal STAI-State; (good versus poor bonding) at 6 weeks postnatal

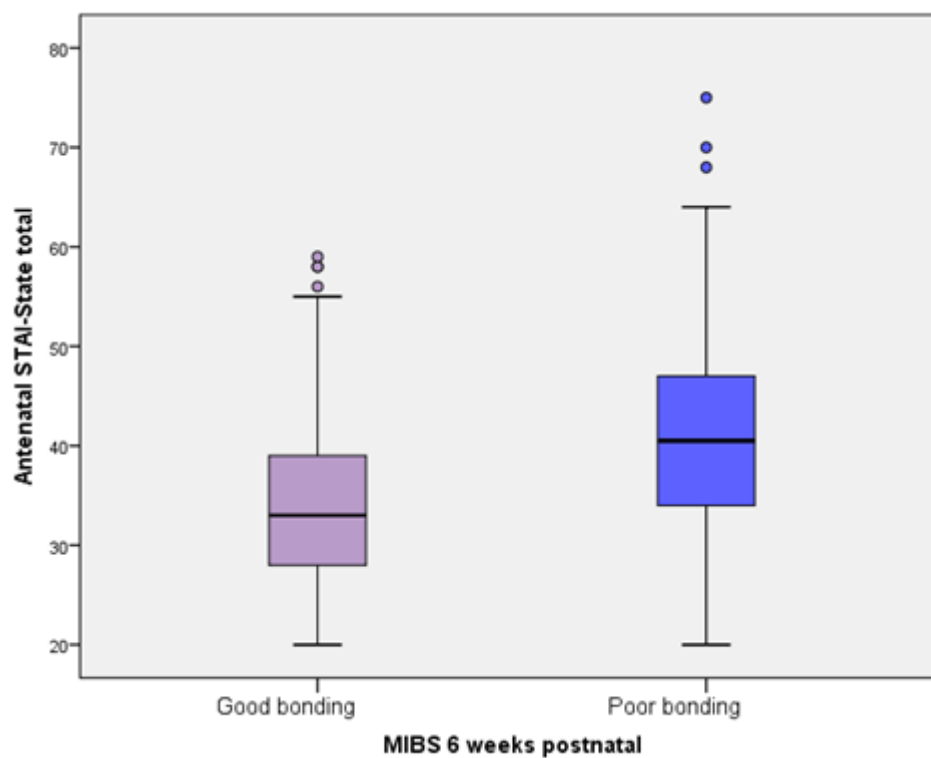
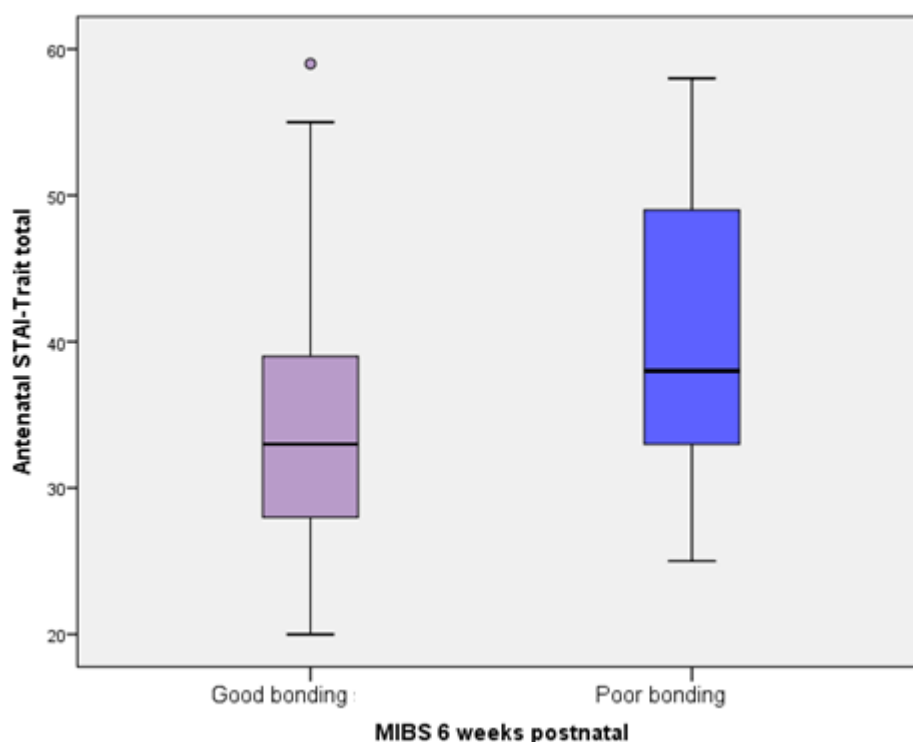


Figure 5-8 Boxplots of antenatal STAI-Trait, (good versus poor bonding) at 6 weeks postnatal



5.5.6 Associations between postnatal psychometric and mother-infant bonding

Spearman rank order correlation showed that the MIBS score at one week postnatal strongly and positively correlated with the score at six weeks postnatal (Spearman rho $n=223$) = 0.70, $p<.001$). A positive correlation was also found between maternal postnatal anxiety, depression and bonding at one and six weeks postnatal, with a positive correlation between maternal personality trait and mother-to-infant bonding at one week, but not six weeks postnatal. No significant correlation was found between the mother-to-infant bonding and maternal postnatal life event scores (table 5.12). In summary, a positive relationship was identified between poor mother-infant bonding and higher

levels of state-trait anxiety and depression, which remained consistent from one week to six weeks postnatal. These results suggest that women with impaired mood bonded poorly with their new infants at one week and that this persisted into the longer postnatal period.

Table 5-12 Postnatal psychometric measures and study outcome

Postnatal psychometric measures	MIBS First week		MIBS 6 weeks	
	correlation coefficient	P-value	correlation coefficient	P-value
MIBS six weeks	0.70	< 0.001		
Postnatal STAI- State	0.34	< 0.001	0.37	< 0.001
Postnatal STAI-Trait	0.33	< 0.001	0.36	< 0.001
Postnatal EPDS	0.39	< 0.001	0.40	< 0.001
Postnatal SLES	0.12	0.082	0.05	0.48
Postnatal SAPAS	0.18	0.008	0.13	0.05

Data are displayed as Spearman correlation coefficients, rho (p value). Abbreviations: MIBS-Mother-to-Infant Bonding Scale, EPDS- Edinburgh postnatal depression scale, SAPAS- standardised assessment of personality abbreviated scale.

Subsequently, the Mann-Whitney U test was used to compare scores of STAI, EPDS, SLES and SAPAS data collected at one and six weeks postnatal between women with good and poor bonding scores, (table 5.13 and 5.14). There was a significant difference in the median scores of all four measures at one and six weeks postnatally. This indicated that women with MIBS ≥ 2 at one and six weeks postnatally experienced higher anxiety and had an increased risk

of postnatal depression than women with MIBS ≤ 2 (indicative of good maternal bonding).

Table 5-13 Difference between women with good bonding and poor bonding scores at one week postnatal on postnatal psychometric measures

Postnatal psychometric measures	Median		Mann-Whitney U	Z	p-value
	Good bonding N=136	Poor bonding N=85			
Postnatal STAI-State	28.0	36.0	3532.5	-4.9	0.001
Postnatal STAI-Trait	31.0	36.0	3672.0	-4.6	0.001
Postnatal EPDS	5.0	9.0	2934.5	-6.2	0.001
Postnatal SLES	1.0	2.0	4743.0	-2.3	.021
Postnatal SAPAS	1.0	2.0	4646.5	-2.5	.012

Table 5-14 Difference between women with good bonding and poor bonding scores at six weeks postnatal on postnatal psychometric measures

Postnatal psychometric measures	Median		Mann-Whitney U	Z	p-value
	Good bonding N=174	Poor bonding N=47			
Postnatal STAI-State	29.0	39.0	2169.5	-4.8	< 0.001
Postnatal STAI-Trait	32.0	40.0	2311.0	-4.4	< 0.001
Postnatal EPDS	5.0	10.0	1778.0	-5.8	< 0.001
Postnatal SLES	1.0	2.0	3095.0	-2.6	0.009
Postnatal SAPAS	1.0	2.0	3120.5	-2.5	0.011

5.6 Logistic regression analysis

5.6.1 Identifying predictors of mother-to-infant bonding

A series of logistic regression models were developed to determine if any significant correlates from the preceding univariate analyses predicted mother-infant bonding outcomes. As explained in Chapter three, the outcome variable was treated as a dichotomous variable (score<2 indicating good bonding; score ≥ 2 indicating poor bonding). The dichotomised (0=good bonding, 1=poor bonding) dependent variable justified the use of binary logistic regression modelling for investigating if significant correlates predicted the likelihood of a mother having poor mother-to-infant bonding at six weeks postnatal (Hosmer et al., 2000, Field, 2009, Menard, 2011).

Bivariate analysis found no associations with demographic data or clinical characteristics between the good and poor mother-infant bonding groups, indicating no need to control for these in the logistic regression analyses.

5.6.2 Antenatal predictors of mother-infant bonding

In the first logistic regression model, the five independent variables were maternal fetal bonding (MAAS), antenatal STAI-State, antenatal EPDS, life events, and SAPAS variables which were significantly correlated with the MIBS. The model chi-square was significant, $\chi^2 (5) = 54.937$, $p < .001$. Indicating that it could distinguish between women who had a good (<2) or poor bonding score (≥ 2).

The model explained between 23% (Cox and Snell R square) and 35% (Nagelkerke R squared) of the difference in mother-to-infant bonding, and

correctly classified 82% of cases meaning that these five independent variables added significantly to the prediction of poor mother-infant bonding. The classification table 5.15 shows the model was wrong for 39 cases (9+30). 94.7% of the good bonding (<2) cases were correctly predicted, but only 33.3% of poor bonding (>=2) cases were correctly predicted.

Table 5-15 Classification table with antenatal psychometric measures

Observed	Predicted		
	Good bonding	Poor bonding	Overall Percentage
Good bonding	162	9	94.7
Poor bonding	30	15	33.3
Overall Percentage			81.9

The result presented in table 5.16, indicated that higher antenatal EPDS depression scores increased the likelihood (odds) of poor mother-infant bonding by 17% (OR=1.171, 95% CI: 1.035-1.326, p=.01). In contrast, a higher antenatal MAAS score decreased the odds of poor mother-infant bonding by 12% (i.e., 1-.878 =, 12) (OR=.878, 95% CI: .831-.928, p=.001). However, antenatal state anxiety, life events, and SAPAS scores were not significant predictors, i.e. they had no effect on poor mother-infant bonding outcomes.

Table 5-16 Results of binary logistic regression predicting poor mother-infant bonding from antenatal psychometric measures at time-point 1

Antenatal predicting variables	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
MAAS	-.13	0.028	21.2	1	<0.001	0.878	0.831	0.928
Antenatal STAI-State	0.01	0.026	0.057	1	0.812	1.006	0.955	1.060
Antenatal EPDS	0.16	0.063	6.280	1	0.012	1.171	1.035	1.326
Antenatal SAPAS	0.13	0.151	0.682	1	0.409	1.133	0.843	1.522
Antenatal SLES	0.08	0.068	1.387	1	0.239	1.083	0.948	1.237
Constant	7.01	2.345						
<i>Total scores of these measures were used against mother-infant bonding score at six weeks as good ≤ 2 and poor bonding score ≥ 2.</i>								

5.6.3 Postnatal predictors of mother-infant bonding

For this analysis, the model included four measures used at six weeks postnatally, the EPDS, STAI-State, SLES and SAPAS scores. The postnatal STAI-Trait variable was omitted from the model due to high inter-correlations with postnatal STAI-State ($\rho = 0.8$, $p < 0.001$). A correlation between each independent variable of > 0.7 is considered too high and indicates a problem with multi-collinearity, which should be avoided in the same analysis (Pallant, 2010) because the two variables might be measuring very similar constructs. The postnatal STAI-State was included as it had a slightly greater effect on bonding scores based on the odds ratios, and was considered a better indicator of maternal anxiety in relation to poor mother-infant bonding.

The model was statistically significant, χ^2 (4df, n = 223) = 42.174, $p < 0.001$, indicating that it could distinguish between a good (< 2) or poor bonding score (≥ 2). The model explained between 17% (Cox and Snell R square) and 27% (Nagelkerke R squared) of the difference in mother-to-infant bonding, and correctly classified 81% of cases. This indicated that the postnatal EPDS score at six weeks postnatal was the only factor predicting mother-infant bonding scores at this time (table 5.17). Higher postnatal EPDS scores increased the likelihood (odds) of poor mother-infant bonding by 22% [OR=1.222, 95% CI: 1.08-1.38, $p < 0.001$]. However, postnatal STAI-State, SLES, and SAPAS scores were not significant predictors and had no effect on poor mother-infant bonding outcomes.

Table 5-17 Results of Binary Logistic regression predicting poor mother-infant bonding from postnatal psychometric measures at six weeks postnatal

Postnatal predicting variables	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Upper
Postnatal EPDS	0.20	0.063	10.1	1	0.001	1.222	1.08	1.38
Postnatal STAI-State	0.02	0.027	0.54	1	0.464	1.020	0.96	1.07
Postnatal SLES	0.02	0.065	0.10	1	0.750	1.021	0.89	1.16
Postnatal SAPAS	0.05	0.137	0.15	1	0.700	1.054	0.80	1.38
Constant	-3.8	0.72				.		
Total scores of these measures were used against mother-infant bonding score at six weeks as good ≤ 2 and poor bonding score ≥ 2								

5.6.4 Relationship between maternal fetal bonding and poor mother-infant bonding, assessing mediating effects

The binary logistic regression analyses found that MAAS, antenatal and postnatal EPDS scores predicted poor mother-infant bonding scores at six weeks postnatal. It was possible that the effect of maternal fetal bonding (MAAS) on poor mother infant bonding was mediated by antenatal and/or postnatal depressive symptoms (as described in Chapter 3, page 108). A moderator is a third variable that changes the relationship between a predictor variable and outcome variable by affecting the strength and direction of this relationship, (Baron and Kenny, 1986, Fairchild and McQuillin, 2010). To assess for possible mediating effects of these variables on mother-infant bonding, bivariate analysis was initially conducted to assess if both MAAS, antenatal and postnatal EPDS were associated with each other. The results (table 5-18), indicated that the MAAS had a negative correlation with the antenatal EPDS (Spearman $\rho=-0.20$, $p<0.003$) and postnatal EPDS score (Spearman $\rho=-0.29$, $p<0.001$); while the antenatal EPDS score was strongly correlated with the postnatal EPDS score ($\rho=.54$, $p<0.001$).

Table 5-18 Associations with statistically significant variables and mother-infant bonding at six weeks postnatal

	MIBS	MAAS	Antenatal EPDS
MAAS	-.456 < 0.001		
Antenatal EPDS	.355 < 0.001	-.201 0.003	
Postnatal EPDS	.492 < 0.001	-.285 < 0.001	.53* <0.001

Following this, a series of logistic regression analysis were developed to assess if the association between the MAAS scores were moderated by maternal antenatal or postnatal depressive symptoms and if the effect of antenatal depressive symptoms on poor mother-infant bonding was moderated by postnatal depressive symptoms. Table 5.19 presents findings, which showed that the relationship between maternal fetal bonding and poor mother-infant bonding remained significant ($p < 0.001$, OR= 0.87-0.89) even after the effect of antenatal and postnatal depressive symptoms had been removed. This indicated that the relationship between maternal fetal bonding during pregnancy and poor mother infant bonding six weeks postnatal was independent and not moderated by symptoms of depression during or after pregnancy.

With regards to antenatal depressive symptoms and mother infant bonding at six weeks postnatal, the p value and odds ratio of antenatal EPDS reduced but did not disappear when postnatal EPDS was added to the model ($p < 0.0005$ to 0.05, OR=1.22 to 1.11) indicating that the relationship between maternal

antenatal depressive symptoms on poor mother-infant bonding was partially mediated by postnatal depressive symptoms.

Table 5-19 Results of possible moderator effect of antenatal and postnatal EPDS on MAAS and MIBS

Potential moderating variables		B	S.E.	Wald	df	Sig.	Exp (B)	95% C.I. for EXP(B)	
								Lower	Upper
Model 1	MAAS	-.135	.026	27.766	1	<.001	0.87	0.83	0.91
Model 2	MAAS	-.127	.028	21.005	1	< .001	0.88	0.83	0.93
	Antenatal EPDS	0.195	.048	16.538	1	< .001	1.21	1.10	1.33
Model 3	MAAS	-.113	.028	15.830	1	< .001	0.89	0.84	0.94
	Antenatal EPDS	0.106	.054	3.814	1	.051	1.11	1.00	1.23
	Postnatal EPDS	0.170	.052	10.521	1	< .001	1.18	1.07	1.31
Total scores of these measures were used against mother-infant bonding score at six weeks as good ≤ 2 and poor bonding score ≥ 2									

5.6.5 Effect of epidural analgesia on poor mother-infant bonding

Bivariate analysis on mode of birth and pain relief in labour presented earlier showed epidural analgesia was associated with poor mother-infant bonding. Pain-relief in labour (coded: 0= no epidural analgesia and 1 epidural analgesia) was added to the final logistic regression model to examine if the effect of antenatal depressive symptoms, maternal fetal bonding or postnatal depressive symptoms on mother-infant bonding were mediated by this. The model also assessed the independent effect of each of these. The model was statistically significant, χ^2 (4df, N 223) =68.841, $p < 0.001$ and explained between 27% (Cox

and Snell R square) and 43% (Nagelkerke R squared) of the variance in mother-to-infant bonding status, correctly classifying 85% of cases.

The four measures remained statistically significant indicating that each was independently associated with predicting impaired mother-infant bonding score at six weeks postnatal. Women who had epidural analgesia were almost three times more likely to have impaired mother-infant bonding at six weeks postnatal, [OR=2.95, 95% CI: 1.08-8.07, $p<.05$] (table 5.20). Antenatal and postnatal depression (EPDS) made a significant but very small contribution to increasing the likelihood of impaired mother-infant bonding [OR=1.12, 95% CI: 1.00-1.24, $p=.05$] and [OR=1.17, 95% CI: 1.06-1.30, $p=.003$], respectively. In contrast, higher maternal fetal bonding scores reduced the likelihood of poor mother-infant bonding by 11% (i.e., 1-0.89) [OR=0.89, 95% CI: 0.84-0.94, $p<.001$], indicating that good maternal fetal bonding may have a positive influence on postnatal mother-infant bonding; whereas antenatal and postnatal depression, and need for epidural have a negative influence on postnatal mother-infant bonding.

Table 5-20 Logistic regression analyses assessing independent predictors of poor mother-infant bonding via pain-relief

Predicting variables	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Upper
MAAS	-.118	.030	15.7	1	<.001	.88	.839	.942
Antenatal EPDS	.109	.055	3.9	1	.046	1.11	1.002	1.242
Postnatal EPDS	.159	.053	9.1	1	.003	1.17	1.057	1.300
Epidural analgesia	1.081	.514	4.4	1	.035	2.94	1.077	8.066
Constant	4.998	2.334						
These measures were used against mother-infant bonding score at six weeks as good ≤ 2 and poor bonding score ≥ 2								

5.7 Additional analysis

5.7.1 Relationship between all antenatal psychometric measures

Pearson correlation (two-tailed) was used to examine possible associations between each of the independent variables and the outcome measures of interest. The correlation coefficients are shown in Table 5.21 (below). Antenatal bonding correlated negatively with state anxiety ($p < .001$), trait anxiety=2 and depression =3, with higher antenatal bonding associated with lower state and trait anxiety and depression. The magnitude of these relationships was weak, with all coefficients below 0.3. Stressful life events did not correlate significantly with antenatal bonding scores. It is also worth noting that state and trait anxiety were strongly, positively correlated with one another, and depression correlated strongly with state and trait anxiety. Overall, these results suggest that pregnant

women in this study population, who had trait (innate) anxiety, were more prone to develop state anxiety and have depressive symptoms during their pregnancy.

Table 5-21 Associations between all antenatal measures

Antenatal psychometric measures	Antenatal bonding (MAAS)	Antenatal STAI- State	Antenatal STAI- Trait	Antenatal EPDS	Antenatal SLES
Antenatal STAI-State	-.268 < .001				
Antenatal STAI-Trait	-.207 .002	.620 <.001			
Antenatal EPDS	-.201 .003	.698 <.001	.658 < .001		
Antenatal SLES	.099 .145	.151 .024	.114 .089	.224 < .001	
Antenatal SAPAS	-.086 .203	.348 <.001	.438 < .001	.363 < .001	.114 .089
*Correlation is significant at the 0.05 level (2-tailed). **Correlation is significant at the 0.01 level (2-tailed).					

5.7.2 Relationship between all postnatal psychometric measures

Spearman correlation (two-tailed) was used to examine possible associations between each of the postnatal psychometric measures (table 5.22). Maternal STAI State and Trait scores were significantly correlated with postnatal EPDS score, a coefficient of 0.7 indicating maternal postnatal anxiety was strongly associated with postnatal depressive symptoms. The postnatal SLES scale was also significantly correlated with postnatal STAI-State & Trait and postnatal EPDS score. However, the relationship was weak, with all coefficients below 0.3.

Table 5-22 Associations between all postnatal psychometric measures

Postnatal psychometric measures	MIBS first week	MIBS 6-weeks	STAI-State	STAI-Trait	EPDS	SLES
MIBS 6weeks	.67 < .001					
STAI-State	.34 < .001	.37 <.001				
STAI-Trait	.33 < .001	.36 < .001	.82 < .001			
EPDS	.38 <.001	.39 <.001	.75 < .001	.72 < .001		
SLES	.12 .08	.05 .44	.24 < .001	.23 .001	.24 < .001	
SAPAS	.18 .008	.14 .031	.37 <.001	.45 < .001	.37 < .001	.15 .020

5.7.3 Section summary

This first part of this section examined the relationship between maternal socio-demographic characteristics, antenatal and postnatal psychometric measures on impaired mother-infant bonding scores at six weeks postnatal. Findings indicated that maternal socio-demographic characteristics did not affect mother-infant bonding in this cohort, but maternal emotional health during and after pregnancy were statistically significantly associated. The antenatal and postnatal scores of all psychometric measures were compared between women with good and poor bonding scores which consistently showed that women with a poor bonding score had higher anxiety and depressive symptoms during and after pregnancy but a lower fetal bonding score during pregnancy.

The predicting effect of maternal fetal bonding, antenatal anxiety and depressive symptoms on poor mother-infant bonding outcome scores at six weeks postnatal were also assessed, which took account of the influence of other factors such as the use of epidural analgesia and postnatal depressive symptoms. The relationship between maternal fetal bonding remained statistically significant with poor mother-infant bonding after taking account of antenatal, postnatal EPDS scores and epidural pain relief. Although the postnatal EPDS score partially reduced the effect size of antenatal EPDS on the MIBS, the result showed a direct statistical significant association between antenatal depressive symptoms and poor mother-infant bonding.

5.8 Section Three: High Risk Pregnancy and Mother– Infant Bonding

This section presents results relevant to assessing if a high risk pregnancy affected mother-infant bonding at six weeks postnatal. Chi-square tests were used to compare scores for categorical variables and Mann-Whitney-U tests were used to test differences in continuous variables.

5.8.1 Socio-demographic characteristics of women with high or low risk pregnancy

Of the 223 women in the study cohort, 157(70%) were classified as having a low risk and 66 (30%) a high risk pregnancy (as defined previously). Socio-demographic comparisons of these two groups are presented in table 5.23. There were no differences in maternal age, ethnicity, being born in the UK, marital status and maternal occupation. However, a trend was found in maternal ethnicity with a higher proportion of Asian women from Asian ethnic group having a medical or obstetric problem in pregnancy.

Table 5-23 Sample characteristics of high and low risk group

Socio-demographic Variables	Total N=223	Low risk Group N=157 (70%)	High risk group N=66 (30%)	Chi-square/ t	P-value
Age		M=33 ±5.1	M= 32±4.5	t= 0.23	0.55
Ethnicity				9.14	0.06
White	152	111(73%)	41 (27%)		
Mixed	14	10 (71%)	4 (29%)		
Asian	23	10(44%)	13 (56%)		
Black	16	12 (75%)	4 (25%)		
Other ethnic group	18	14 (78%)	4 (22%)		
Born in UK				0.06	0.80
Yes	129	90(70%)	39(30%)		
No	94	67(71%)	27(29%)		
Education				6.1	0.10
O'LEVELS/GCSEs	19	9(47%)	10(53%)		
A LEVELS/ vocational training	16	12(75%)	4(25%)		

Socio-demographic Variables		Total N=223	Low risk Group N=157 (70%)	High risk group N=66 (30%)	Chi-square/ t	P-value
	Degree	91	63(69%)	28(31%)		
	Higher degree	97	73(75%)	24(25%)		
Marital status					2.75	0.25
	married	159	110 (69%)	49 (31%)		
	living with partner	52	36(69%)	16(31%)		
	Alone	12	11(92%)	1(8%)		
Maternal occupation					3.1	0.37
	Professional	100	74 (74%)	26(26%)		
	Managerial	49	35(71%)	14(29%)		
	Skilled/unskilled	35	25(71%)	10(29%)		
	Others (Housewife, student)	39	23(59%)	16 (41%)		

5.8.2 Labour, birth and neonatal outcomes

Labour, birth and neonatal outcome data were available for the 223 women with complete data and comparisons between the two groups presented in tables 5.24 and 5.25. Statistically significant differences were found in birth complications between the groups and gestational age at birth.

Table 5-24 Labour and birth outcomes between high and low risk pregnancy groups

Labour and birth outcomes	Total 223	Low risk 157 (70%)	High risk 66 (30%)	P value
Mode of delivery				0.30
Spontaneous delivery	96 (43%)	69 (43%)	27(42%)	
Instrumental delivery	48 (21%)	30 (19%)	18 (26%)	
Elective caesarean section	44 (20%)	35 (23%)	9 (14%)	
Emergency caesarean section	35(16%)	23 (15%)	12 (19%)	
Pain relief in labour				0.44
Epidural	154 (69%)	106 (67%)	48 (73%)	
No epidural	69 (31%)	51 (33%)	18 (27%)	
Birth complication				0.002
No complication	172 (77%)	130 (83%)	42 (64%)	
Yes complication	51(23%)	27(17%)	24 (36%)	
Gestational age at birth				0.004
Preterm birth	78(4%)	2(1%)	6 (9%)	
Term	215 (96%)	155 (99%)	60 (91%)	

Statistically significant differences were found in birth weight and head circumference between the low and high risk groups. Low risk mothers delivered heavier babies with larger head circumference.

Table 5-25 Neonatal outcomes between high and low risk pregnancy groups

Labour, delivery, birth and neonatal outcome variables	Low risk 157 (70%)	High risk group 66 (30%)	P value
Birth weight	M=3484gm SD=537	M=3181gm SD= 592	0.00
Head circumference	M=35cm SD=1.67	M=34cm SD=1.58	0.01
Apgar at 1 minute	M=8.49 SD=1.17	M=8.28 SD=1.53	0.27
Apgar at 5 minutes	M=9.69 SD=0.58	M=9.57 SD= 0.76	0.22
Sex of baby			0.29
Boy	81 (52%)	29 (44%)	
Girl	76 (48%)	37 (56%)	

5.9 Antenatal psychometric measure outcomes between women with high and low risk pregnancies

The total scores of antenatal psychometric measures used during pregnancy were compared between the two groups (table 5.26). A significant difference was found with STAI-State anxiety score but not with STAI-Trait or other measures used. Women with high risk pregnancies had a higher median score ($Md=36$, $n=66$) than low risk women ($Md=33$, $n=157$) in antenatal STAI-State but not the STAI-Trait, EPDS, SLES, MAAS or antenatal SAPAS scores. This finding indicated that perhaps not unexpectedly women with a high risk pregnancy had higher anxiety during pregnancy than those with a low risk pregnancy, but similar trait anxiety, depressive symptoms and fetal bonding.

Table 5-26 Antenatal measure outcomes for women with high and low risk pregnancies

Antenatal psychometric Measures	Median		Mann-Whitney U	Z	Asymp. Sig. (2-tailed)
	Low Risk	High Risk			
MAAS	80	81	4607.0	-.829	.407
Antenatal STAI-State	33	36	4087.0	-2.456	.014
Antenatal STAI-Trait	33	35	4595.5	-1.301	.193
Antenatal EPDS	5	6	4636.5	-1.211	.226
Antenatal SLES	1	1	4534.0	-1.487	.137
Antenatal SAPAS total	2	2	4877.0	-.678	.498

5.9.1 Antenatal anxiety, depression and poor maternal fetal attachment

There was a statistically significant difference in the Spielberger State Anxiety score ($\chi^2 = 4.9$, $p = 0.03$) but not Spielberger Trait anxiety ($\chi^2 = 0.00$, $p = 0.98$) between the high and low risk pregnancy groups (table 5.27). Around 42% of women with a high risk pregnancy had a Spielberger State Anxiety score of 40 or more compared with 27% of the women with a low risk pregnancy. There was no difference between the groups in the proportion of women who had an EPDS score of ≥ 13 or proportion of women at risk of poor maternal-fetal attachment ($\chi^2 = 0.85$, $p = 0.23$).

Table 5-27 Differences in antenatal anxiety, depressive symptoms and poor maternal fetal attachment between high and low risk pregnancy groups

Antenatal Psychometric measures	Total	Low risk 157 (70%)	High risk 66 (30%)	Chi-square	P-Value
STAI-State				4.9	0.03
Total score <40	152(68%)	114 (73%)	38 (58%)		
Total score ≥40	71 (32%)	43(27%)	28 (42%)		
STAI-Trait				.00	0.98
Total score<40	162 (73%)	114 (73%)	48 (73%)		
Total score≥40	61 (27%)	43 (27%)	18 (27%)		
EPDS				2.24	0.13
Total score<13	203 (91%)	140(89%)	63 (95%)		
Total score≥13	20 (9%)	17(11%)	3 (5%)		
MAAS				0.85	0.23
Total score<76	50 (23%)	38 (24%)	12 (19%)		
Total score≥76	168 (77%)	117 (76%)	52(81%)		

5.10 Postnatal psychometric measures between women with high and low risk pregnancies

There were no statistically significant differences between the two groups in mother-to-infant bonding scores at one or six weeks postnatal or their postnatal STAI-state-trait anxiety, EPDS, SLES and SAPAS scores. However there was a trend among women who had a high risk pregnancy and higher levels of anxiety during the postnatal period (table 5.28).

Table 5-28 Postnatal psychometric measures between women with high and low risk pregnancies

Postnatal psychometric Measures	Median		Mann-Whitney U	Z	P-value
	Low Risk	High Risk			
MIBS first week	0.9	0.9	5064.0	-.058	.954
MIBS 6 weeks	0.5	0.4	4922.5	-.440	.660
Postnatal STAI-State	31	35	4290.5	-1.831	.067
Postnatal STAI-Trait	33	35	4271.0	-1.876	.061
Postnatal EPDS	6	7	4438.0	-1.495	.135
Postnatal SLES	1	2	4397.5	-1.801	.072
Postnatal SAPAS	2	2	4420.5	-1.575	.115

5.10.1 Postnatal anxiety and depression in high and low risk pregnancy groups

The proportion of women at risk of poor mother-infant bonding at six weeks postnatal and outcome of psychological measures including EPDS \geq 13 and STAI State-Trait \geq 40 were compared (table 5.29). The proportion of women with a high risk pregnancy at risk of impaired mother-infant bonding (MIBS score \geq 2) was not statistically different from those with a low risk pregnancy at six weeks postnatal, or for an EPDS \geq 13. Although the number of women with a Spielberger State-Trait anxiety score of 40 or more was higher in women with a high risk pregnancy, this did not reach statistical significance.

Table 5-29 Differences in proportions of poor mother-infant bonding, postnatal anxiety and depressive symptoms between high and low risk pregnancy groups

Postnatal psychometric variables	Total	Low risk pregnancy 159 (71%)	High risk pregnancy 65 (29%)	Pearson Chi-Square	P-value
MIBS first week				0.29	0.58
Score<2	136	99 (73%)	37 (27%)		
Score≥2	85	59 (69%)	26 (31%)		
MIBS 6 weeks				0.30	0.58
Score<2	176	127 (72%)	49 (28%)		
Score≥2	47	32 (68%)	15 (32%)		
Postnatal Spielberger State				1.69	0.19
Total score <40	171	125 (73%)	46 (27%)		
Total score ≥40	53	34 (64%)	19 (36%)		
Postnatal Spielberger Trait				1.48	0.22
Total score<40	161	118 (73%)	43 (27%)		
Total score≥40	63	41(65%)	22 (35%)		
Postnatal EPDS				0.50	0.47
Total score<13	197	142 (72%)	55 (28%)		
Total score≥13	26	17 (65%)	9 (35%)		

5.10.2 Summary

The results presented in this section showed no significant differences between women with a high and a low risk pregnancy and any of the psychometric measures completed in the postnatal period. Although women with a high risk pregnancy had higher anxiety and depression during pregnancy, their maternal antenatal attachment, postnatal depression and mother-to-infant bonding scores remained similar, indicating that a high risk pregnancy did not affect mother to infant bonding in this population sample.

5.11 Section Four: Pilot Study Results

This section presents the results of the 'nested' pilot study completed to explore the feasibility of collecting maternal salivary cortisol and alpha amylase in late pregnancy and potential association with anxiety, depression and impaired mother-infant bonding at six weeks postnatal. If findings indicated, a substantive future project could be planned to use biomarkers to identify women at risk of poor infant bonding.

The response rate and socio-demographic characteristics of participants will be presented first followed by the results of salivary cortisol and alpha-amylase analysis. This includes the diurnal patterns of salivary cortisol, the difference in diurnal patterns between two groups (EPDS score \leq and \geq 13; MIBS \leq and \geq 2), associations with self-reported maternal symptoms of anxiety, depression, and mother-infant bonding. The salivary alpha amylase results will be reported similarly.

5.11.1 Response rate

As reported previously, 120 (56%) women provided an antenatal saliva sample at 36 weeks gestation out of a total of 215 women recruited to the pilot study. Fifty-five (46%) women returned postnatal samples out of the 120 women who returned their antenatal saliva samples. There were several reasons for missing data. These included failure by women to return postnatal saliva samples (n=65); poor compliance or incorrectly collection of the sample as directed, leading to insufficient samples for analysis (n=7). The results of two participants

were excluded from analysis as they were receiving treatment for severe depression at six weeks postnatal which was a study exclusion criterion.

5.11.2 Characteristics of study participants with biological data

The socio-demographic characteristics of participants who provided antenatal and postnatal saliva sample (n = 46) are presented in table 5.30. Mean maternal age was 33 (SD = 4.56; range, 23-44). Most women (38, 83%), were white and just over half were born in the United Kingdom. A higher proportion of women who provided antenatal and postnatal saliva samples were married. Just under half had attended higher education with 22 (48%) educated to undergraduate degree and 19 (41%) to masters or PhD level.

Table 5-30 Socio-demographic characteristics of pilot study sample

Socio-demographic variables	Antenatal data (n=77)	Antenatal and postnatal data (n=46)
Maternal mean age	33	33
Standard deviation	4.8	4.5
Range	22-43	23- 44
Age groups		
≤30	27 (35%)	11 (24%)
31 - 34	27 (35%)	21 (46%)
35+	23 (30%)	14 (30%)
Ethnicity		
White	60 (78%)	38 (83%)
Non white	17 (22%)	8 (17%)
Born in UK		
Yes	42 (59%)	25 (54%)
No	29 (41%)	21 (46%)
Maternal education		
O'Level's / A 'level equivalent	12 (16%)	5 (11%)
Degree	35 (46%)	22 (48%)
Higher degree (Masters/ PhD)	30 (39%)	19 (41%)
Maternal occupation		
Professional	34 (44%)	25 (54%)
Managerial	19 (25%)	11 (24%)
Other	24 (31%)	10 (22%)
Marital status		
Married	48 (62%)	32 (67%)
Not married	29 (38%)	14 (30%)

Data are displayed as numbers, % percentages

5.12 Maternal salivary cortisol

Cortisol levels in the maternal saliva samples were based on samples collected by women immediately upon waking, as well as 30 minutes, 8 hours and 12 hours post waking, for two consecutive days at 36 weeks gestation and six weeks postnatal. Cortisol levels were measured using a competitive enzyme immunoassay.

Initially, all biochemical data were tested for normal distribution using normal probability (P-P plot) from SPSS version 20; to determine if parametric or non-parametric statistics should be used. Analyses was conducted using parametric tests, except when assessing mother-infant bonding score results as previous research has demonstrated that these data are highly skewed and did not follow a normal distribution, (Taylor et al., 2005).

5.12.1.1 Antenatal and postnatal salivary cortisol Day 1 and 2

A paired-sample t-test analysis was used to compare cortisol values between samples collected on days 1 and day 2 during the antenatal and the postnatal periods. Antenataly there was a significant correlation with antenatal cortisol collected at the same time on days 1 and 2 ranging from $r = 0.32 - 0.63$, $p < 0.001 - 0.01$, $n = 61$. A significant correlation was also found between the values of the postnatal samples collected on waking and at 8 and 12 hours post waking on days 1 and 2, ranging from $r = 0.44 - 0.64$, $p < 0.001 - 0.006$, but not for 30 minutes post waking ($n = 38$, $r = 0.25$, $p > 0.05$, ns). As there were no significant differences in antenatal and postnatal salivary cortisol results

between day 1 and day 2 at any time point the mean values of day 1 and 2 cortisol levels were used in subsequent analyses.

5.12.1.2 Association between maternal salivary cortisol at time-point 1 and time-point 2

A paired-sample t-test analysis was also used to compare cortisol values between samples collected during the antenatal and the postnatal periods. Paired sample mean between antenatal cortisol at 36 weeks gestation and six weeks postnatal are presented in table 5.31.

Table 5-31 Paired sample mean antenatal and postnatal cortisol

Antenatal and postnatal cortisol		N	Mean	Std. Deviation
Waking	Antenatal	45	10.34	4.06
	Postnatal	45	7.65	4.48
+30 minutes	Antenatal	46	12.74	4.67
	Postnatal	46	7.51	3.34
+8hours	Antenatal	47	5.42	2.25
	Postnatal	47	1.83	0.89
+12 hours	Antenatal	46	3.80	1.34
	Postnatal	46	1.50	1.55

There was a significant correlation between antenatal cortisol and postnatal cortisol at waking, +30 minutes and +12 hours, ranging from $r = 0.37- 0.47$, $p < 0.001- 0.01$, $n = 45$, but no significant correlation between the antenatal and postnatal 8 hours post waking samples ($r = 0.24$, $p > 0.1$, $n = 47$). There was a

significant difference between antenatal and postnatal salivary cortisol (table 5.32) indicating a significant decrease in salivary cortisol measures from antenatal to postnatal at each time point.

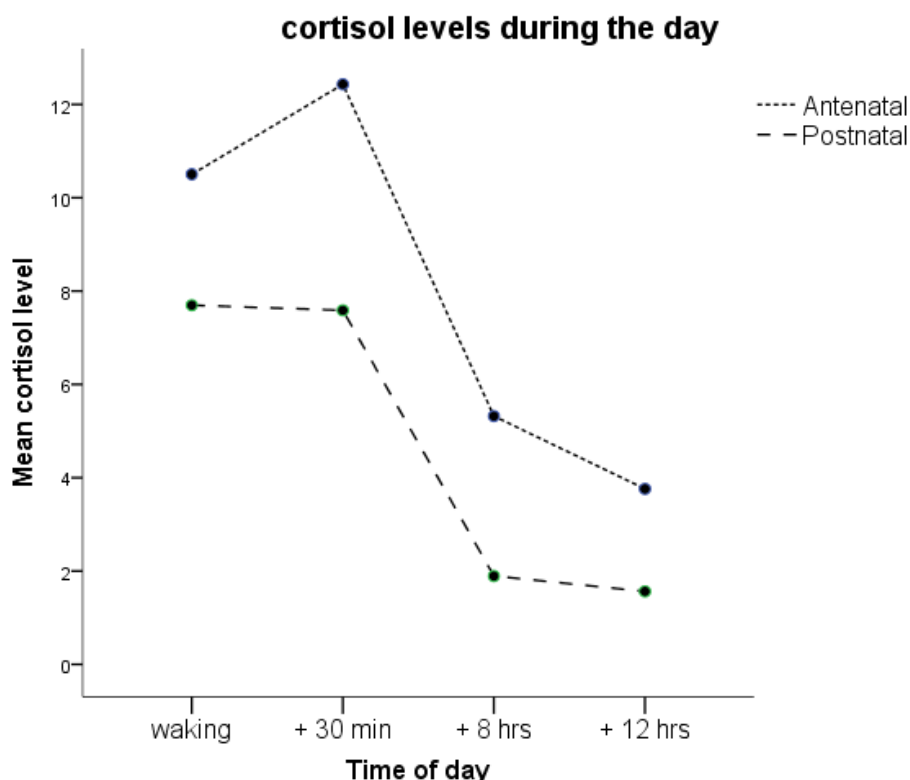
Table 5-32 Antenatal and postnatal salivary cortisol

Antenatal and postnatal salivary cortisol	Mean difference	SD	t	P value	95% C. I of the Difference	
					Lower	Upper
Waking	2.7	4.8	3.7	0.001	1.2	4.1
+30 minutes	5.2	4.5	8.0	< 0.001	3.9	6.6
+ 8 hours	3.6	2.2	11.1	< 0.001	2.9	4.2
+12 hours	2.3	1.5	10.4	< 0.001	1.9	2.8

5.12.2 Antenatal and postnatal cortisol diurnal profile

The expected diurnal profile with a marked cortisol awakening response (CAR) followed by a continuous decline throughout the day was observed in the antenatal samples, but not in the postnatal samples with no waking peak identified (cortisol awakening response, fig 5.9).

Figure 5-9 Differences in the antenatal and postnatal cortisol diurnal profile, tested using a repeated measure ANOVA



5.12.2.1 Cortisol diurnal profile between two groups (EPDS \leq and \geq 13)

A two-way ANOVA explored changes in the maternal saliva samples collected at the different times of day at 36 weeks gestation and six weeks postnatal between the groups with lower (≤ 13) and higher (≥ 13) EPDS scores. There was a significant effect of time of day during the antenatal period ($P < 0.0005$) and postnatal period ($P < 0.0005$) but no significant interaction effect between the two groups during the antenatal period ($p = 0.6$) or postnatal period ($p = 0.5$). This suggested that the diurnal profile between the two groups was similar in both the antenatal and postnatal periods (figures 5.10 and 5.11). However women with higher EPDS scores had a reduced cortisol mean during waking and throughout the day compared with women with EPDS scores ≤ 13 (table 5.33). This suggests that lower cortisol levels may be associated with higher risk of

postnatal depression in contrast to pregnancy when higher levels of maternal cortisol may be associated with risk of depression.

Figure 5-10 Diurnal cortisol profile and EPDS score during pregnancy

Antenatal cortisol diurnal pattern (antenatal EPDS<13 verse EPDS=>13)

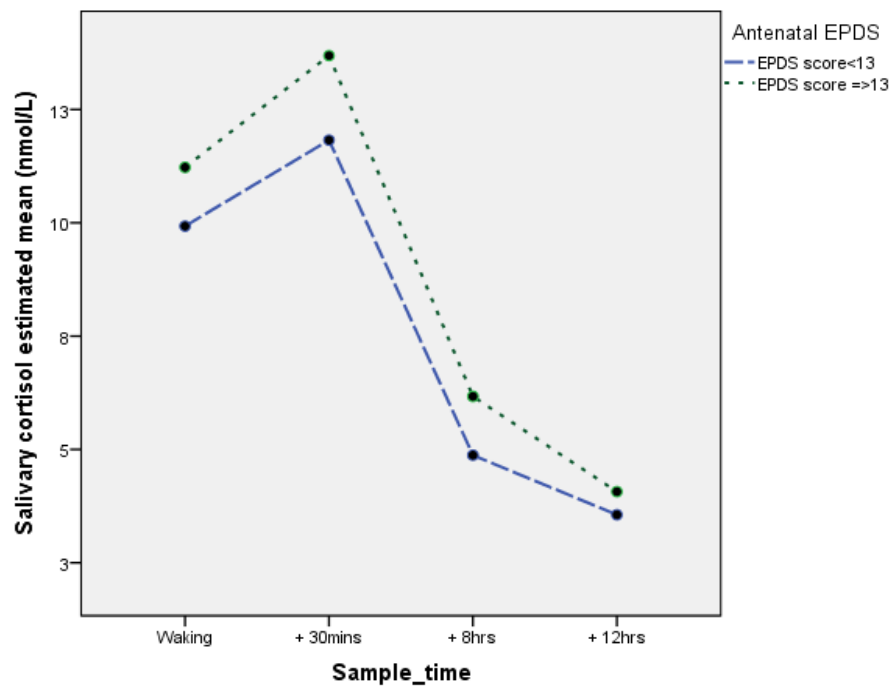


Figure 5-11 Diurnal cortisol profile and EPDS score at 6 weeks postnatal

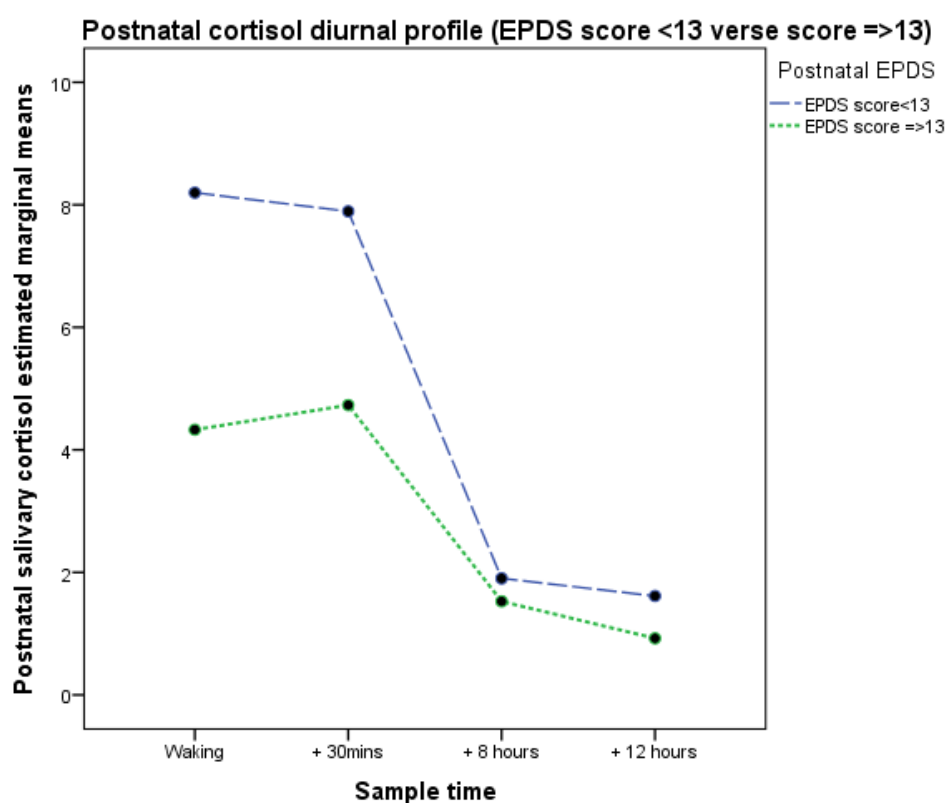


Table 5-33 Antenatal and postnatal salivary cortisol mean (EPDS≤13 versus ≥13)

Salivary cortisol 36 weeks gestation	Antenatal EPDS<13 N=61		Antenatal EPDS ≥13 N=10	
	Mean	SD	Mean	SD
Waking	9.9	3.4	11.1	5.5
+30 mins	11.6	4.3	13.2	5.0
+8 hours	4.7	1.7	5.6	3.0
+12 hours	3.4	1.2	3.9	1.6
Salivary cortisol 6 weeks postnatal	n=39		n=3	
waking	8.2	4.5	4.3	2.8
+30 mins	7.9	3.4	4.7	2.9
+8 hours	1.9	0.9	1.9	0.9
+12 hours	1.6	1.7	0.9	0.3

5.12.2.2 Cortisol diurnal profile between and good and poor mother-infant bonding score

A two-way ANOVA was conducted to explore changes in the maternal saliva sample collected at different times of day at 36 weeks gestation and six weeks postnatal between women with good and poor mother-infant bonding scores at six weeks postnatal. An expected main effect of time-point was evident between the antenatal and postnatal salivary cortisol ($P < .0005$), suggesting a significant change in cortisol levels from the antenatal to the postnatal period. No significant effect was found for mother-infant bonding status (antenatal period $F(3, 51) = 0.88, p = 0.5$); (postnatal period, ($F(3, 38) = 1.57, p = 0.2$)).

Although the diurnal profile was similar between the groups, the normal cortisol awakening response (CAR, an increase in cortisol secretion between the moment of waking and 30mins later) was evident in both groups antenatally (fig.5.12), but absent in women with a good bonding score six weeks postnatally (fig.5.13). Furthermore, the estimated margin mean in repeated ANOVA (table 5.34) showed that women with a poor bonding score (score ≥ 2) had a slightly higher mean at +30mins post waking during the antenatal period and three time points (waking, +30mins and +8hours) than those with a good score (score < 2) postnatally, but differences were not statistically significant.

The salivary cortisol mean between women who scored above the threshold of probable poor bonding ≥ 2 and those below ≤ 2 is presented in table 5.34.

Figure 5-12 Antenatal diurnal cortisol profile between women with good and poor bonding scores at 6 weeks postnatal

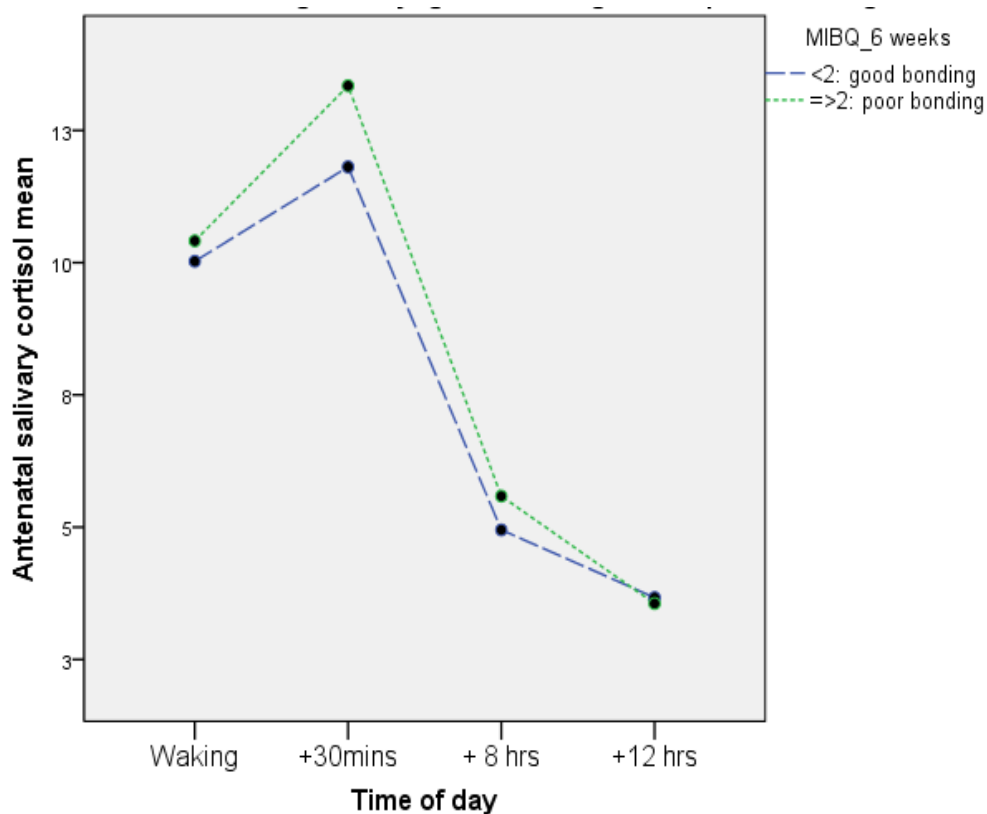


Figure 5-13 Postnatal salivary cortisol diurnal profile in women with good and poor bonding scores at 6 weeks postnatal

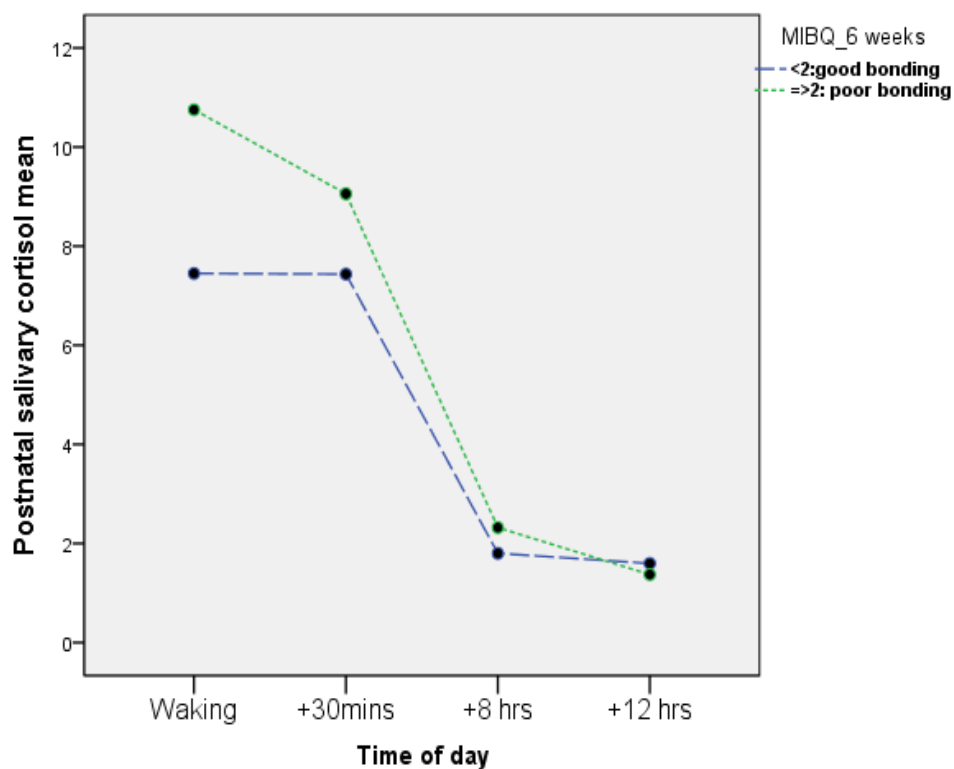


Table 5-34 Maternal salivary cortisol estimated margin mean and standard deviation (good bonding versus poor bonding scores)

Salivary cortisol 36 weeks gestation	MIBS <2 N=44		MIBS ≥2 N=11	
	Mean	SD	Mean	SD
waking	10.02	3.8	10.4	4.9
+30 mins	11.8	4.1	13.3	5.8
+8 hours	4.9	1.8	5.6	2.6
+12 hours	3.7	1.3	3.6	1.1
Salivary cortisol 6 weeks postnatal	n=36		n=6	
waking	7.4	4.3	10.6	5.2
+30 mins	7.4	3.6	9.1	1.7
+8 hours	1.8	0.9	2.3	1.0
+12 hours	1.6	1.7	1.4	1.3

5.12.3 Associations between maternal salivary cortisol and self-reported measures of maternal anxiety and depression

5.12.3.1 Spielberger State-Trait anxiety and maternal salivary cortisol

There was no association with maternal anxiety as measured at 36 weeks gestation using the Spielberger State & Trait anxiety inventory scale and maternal salivary cortisol collected at 36 weeks gestation or six weeks postnatal.

5.12.3.2 Edinburgh Postnatal Depression Scale and maternal salivary cortisol

Similarly, a correlation analysis to explore the relationship between maternal depressive symptoms assessed using the EPDS and salivary cortisol from 36 weeks gestation and six weeks postnatal showed no correlation between antenatal or postnatal EPDS total scores.

5.12.3.3 Maternal salivary cortisol and mother-infant bonding score

Spearman non-parametric analysis was used to explore the association between maternal cortisol and self-reported measures of maternal anxiety and depression during pregnancy and six weeks postnatal, which showed no significant correlation between mother-infant bonding and maternal salivary cortisol at any time of the day.

5.13 Maternal salivary alpha-amylase

Similar to salivary cortisol, maternal alpha amylase levels were based on saliva samples collected by women immediately upon waking, as well as 30 minutes, 8 hours and 12 hours post waking for two consecutive days (day1 and 2) at 36 weeks gestation and 6 weeks postnatal. As described in Chapter four, maternal salivary alpha-amylase levels were measured using a kinetic enzyme assay.

5.13.1 Antenatal and postnatal salivary alpha-amylase days 1 and 2

A paired-sample t-test analysis was used to compare alpha amylase values between samples collected on days 1 and day 2 during the antenatal and the postnatal periods. There was a highly significant correlation between the values of antenatal salivary alpha-amylase collected at the same time on days 1 and 2, ranging from $r = 0.36$ to 0.62 , $p < 0.001$ to 0.02 , $n = 68$. There were also significant correlations between postnatal samples collected at the same time on days 1 and 2, ranging from $r = 0.35$ to 0.60 ; $p < 0.001$ to 0.05 , $n = 43$.

5.13.1.1 Maternal salivary alpha-amylase at time-point 1 and time-point 2

Antenatal and postnatal alpha-amylase were highly significant correlated at 30 minutes up to 12 hours post waking, ranging from $r = 0.3.7$ to 0.46 , $p < 0.001$ to 0.01 , $n = 48$). No significant correlation was found for the waking sample, ($r = 0.28$, $p < 0.07$, $n = 46$). Paired-sample t-tests showed no statistically significant difference between antenatal and postnatal salivary alpha-amylase at any time point (table 5.35), indicating that maternal salivary alpha-amylase is stable and does not change from antenatal to postnatal, unlike maternal cortisol which had a significant drop from antenatal to postnatal period.

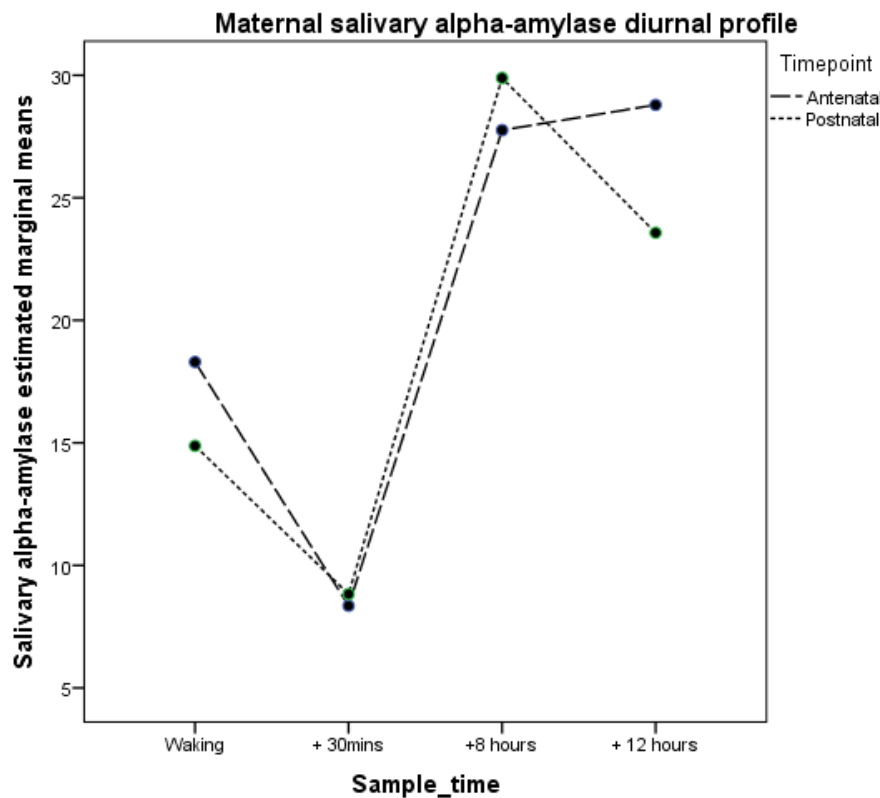
Table 5-35 Paired sample differences between maternal antenatal and postnatal salivary alpha-amylase

Antenatal and postnatal alpha-amylase	Mean	SD	95% C I of the Difference		t	P value
			Lower	Upper		
Waking	3.3	22.6	-3.4	10.0	1.0	0.3
+30mins	-.13	11.3	-3.6	3.2	-0.1	0.9
+8 hours	-2.9	25.6	-10.2	4.5	-0.8	0.4
+12 hours	3.4	28.9	-5.09	11.9	0.8	0.4

5.13.2 Salivary alpha-amylase diurnal profile

The diurnal profile of salivary alpha-amylase is shown in figure 5.14. Salivary alpha-amylase demonstrated a reduction in 30mins post waking; it increased above waking levels by 8 hours post waking. A similar profile was found in both the antenatal and postnatal samples, but there was a non-significant decline in postnatal levels after 8 hours post-waking.

Figure 5-14 Antenatal and postnatal alpha-amylase diurnal profile



5.13.2.1 Alpha-amylase diurnal profile between good and poor bonding groups

Analysis of variance was used to test the effect of antenatal and postnatal maternal salivary alpha-amylase sample collected across the day on mother to infant bonding scores at six weeks postnatal. The data were analysed using a mixed-design ANOVA with a within-subjects factor of sample collection time (waking, +30mins, + 8hours and 12 hours post waking) and a between-subject factor of mother-to-infant bonding status (good bonding: score<2; poor bonding: score≥2). There was no effect of sample collection time on mother-to-infant bonding scores, $F(3, 51) = 2.17$, $p = 0.10$, with antenatal salivary alpha-amylase and $F(3, 37) = 0.90$, $p = 0.25$ with postnatal salivary alpha-amylase. The alpha-amylase diurnal profile in women with poor bonding scores was

similar to those of women with good scores. However, the latter had a higher estimated mean across the day during the antenatal period (figure 5.15) and a higher postnatal mean at, 8 and 12 hours post waking (figure 5.16), Mean values between the two groups are presented in table 5.36.

Figure 5-15 Antenatal diurnal alpha-amylase profile between women with good and poor bonding scores

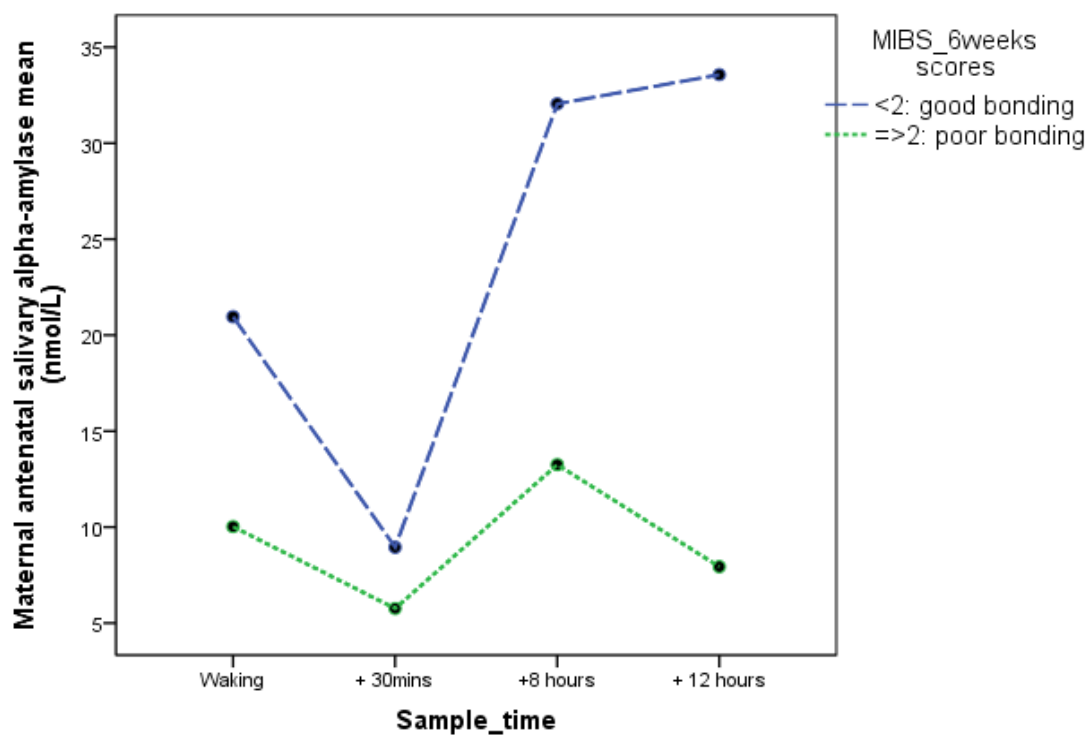


Figure 5-16 Postnatal diurnal alpha-amylase profile between women with good and poor bonding scores at six weeks postnatal

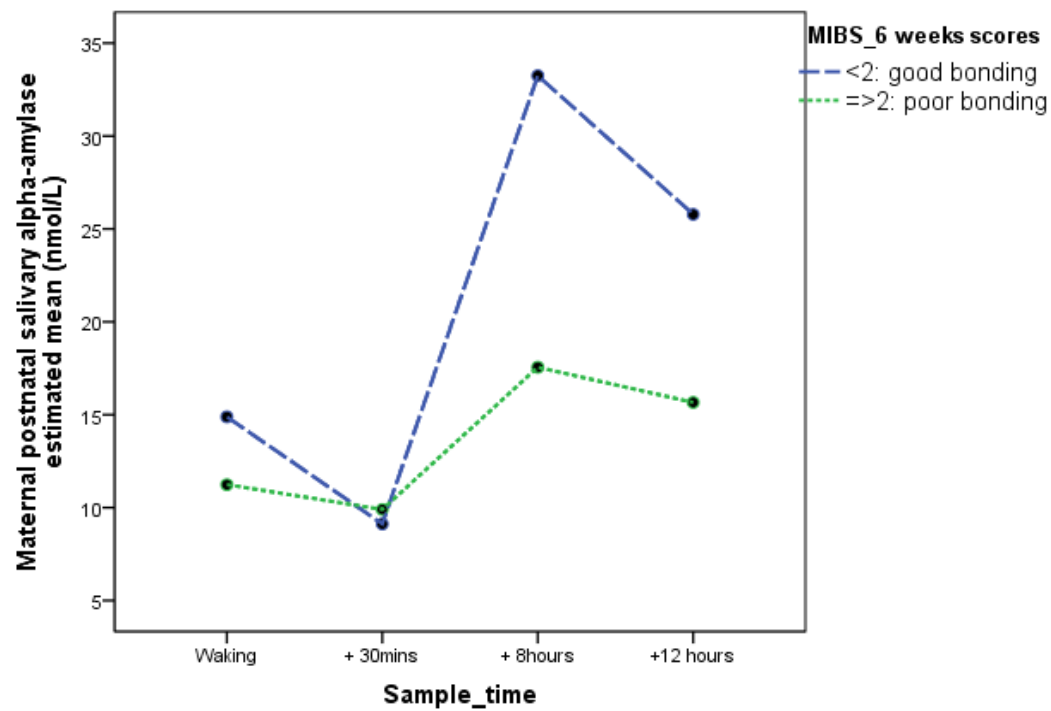


Table 5-36 Maternal salivary alpha-amylase estimated margin mean (good versus poor bonding)

Antenatal salivary alpha-amylase 36 weeks gestation	MIBS <2 N=40		MIBS ≥2 N=11	
	Mean	SD	Mean	SD
Waking	24.0	28.4	14.6	17.6
+30 mins	9.9	11.4	9.4	10.2
+8 hours	29.1	23.5	21.3	23.9
+12 hours	26.5	22.4	14.6	11.9
Postnatal salivary alpha-amylase 6 weeks	n=31		n=7	
Waking	12.4	10.4	11.2	9.3
+30 mins	7.2	6.5	9.9	16.9
+8 hours	29.4	21.8	17.6	13.3
+12 hours	22.0	15.8	15.7	7.9

5.13.3 Maternal salivary cortisol and alpha-amylase

A Pearson correlation analysis was used to examine association between maternal salivary alpha-amylase and cortisol in the study population, but no correlation was found for any time points during or after pregnancy.

5.13.4 Associations between maternal salivary alpha-amylase and self-reported measures of maternal anxiety and depression

No correlation was found between the EPDS, the STAI and maternal salivary alpha-amylase at any time point. However, a significant correlation was found between antenatal STAI anxiety and postnatal alpha-amylase at 8 hours post-waking ($r = -0.30$, $p < 0.04$, $n = 48$), antenatal STAI trait with postnatal alpha-amylase at 8, ($r = -0.31$, $p < 0.03$, $n = 48$), and 12 hours post waking, ($r = -0.35$, $p < 0.02$, $n = 48$). There was no correlation found between postnatal STAI anxiety and antenatal or postnatal alpha-amylase. A statistically significant correlation was found between postnatal STAI trait and postnatal alpha-amylase at 12 hours post waking ($r = -0.36$, $p < 0.02$, $n = 48$), but not at any other time point.

5.13.5 Association between mother-infant bonding score and maternal salivary alpha-amylase

Spearman correlation analysis was used to identify possible association between values of maternal salivary alpha-amylase collected antenatally and postnatally and results of the MIBS completed at one and six weeks postnatally. There was a statistical significant correlation with MIBS at six weeks postnatal,

and antenatal maternal salivary alpha-amylase at the 12 hours post waking time point but not at any other time (table 5.37) this negative correlation, suggesting higher antenatal amylase was associated with better postnatal bonding.

Table 5-37 Maternal salivary alpha-amylase and MIBS at one and six weeks

Saliva sample collection	MIBS First week			MIBS 6 weeks	
	N	Correlation	P value	Correlation	P value
Antenatal alpha-amylase					
Waking	60	0.02	0.9	-0.13	0.3
+30mins	59	-0.06	0.6	-0.09	0.5
+8 hours	61	-0.13	0.3	-0.17	0.2
+12 hours	60	-0.18	0.2	-0.35**	0.01
Postnatal alpha-amylase					
Waking	43	0.08	0.6	-0.04	0.8
+30mins	43	-0.14	0.4	-0.16	0.3
+8 hours	45	-0.25	0.1	-0.28	0.1
+12 hours	45	-0.03	0.8	-0.21	0.2

5.13.6 Summary

Antenatal alpha-amylase collected at twelve hours post waking was negatively correlated with the MIBS at six weeks postnatal, and non-significant negative correlations at the other antenatal times of day. Bonding in the first week postnatal did not show any correlations with antenatal alpha-amylase. No significant correlations were identified between postnatal alpha-amylase data, and MIBS scores, although there was a trend for higher amylase to be

associated with better bonding. The negative correlations observed between antenatal alpha-amylase and bonding at six weeks postnatally suggest that higher antenatal alpha-amylase levels were associated with good mother-infant bonding at this time.

The alpha-amylase diurnal profile of women with good bonding was similar to women with poor bonding although women with good bonding scores appeared to have higher alpha amylase mean in both time points.

There was no association between antenatal or postnatal cortisol and the MIBS score at one week postnatally and bonding at six weeks postnatally and no significant correlation between cortisol and alpha-amylase during the antenatal or postnatal periods.

CHAPTER 6 DISCUSSION AND CONCLUSION

6.1 Introduction

A prospective cohort study was presented in this thesis which aimed to identify factors in pregnancy that could predict early mother-infant bonding problems at six weeks postnatal. It included data on 461 women in pregnancy, 223 of who were followed up to six weeks postnatal. Data were also presented from a 'nested' pilot study of 46 women who provided salivary samples at 36 weeks gestation and six weeks postnatal in order to assess whether biological measures of stress in maternal saliva could be used as a tool to predict poor mother-to-infant bonding.

The aims and objectives of the main study were met, namely to: examine whether risk of high depressive symptoms or other psychological problems in late pregnancy predicted poor mother-to infant bonding at six weeks postnatal; whether psychometric measures of postnatal anxiety or depression would correlate with scores on the MIBS and finally if mother-infant bonding or other psychometric scores differed between women who had a high or a low risk pregnancy as defined by NICE (2007).

Completion of the nested pilot study of whether measuring two stress hormones (cortisol and alpha-amylase) in maternal salivary samples in late pregnancy could be used as a method of predicting poor mother-to infant bonding at six weeks postnatal indicated that assessment of saliva cortisol measures to predict bonding outcomes is unlikely to be of benefit. However,

the finding of a possible association between maternal salivary alpha-amylase and mother infant bonding is a preliminary finding, warrants a larger study to confirm the finding.

In this chapter, study findings are discussed in relation to the research aims, objectives, hypotheses, and previous literature on impaired mother to infant bonding. Consideration is also given to areas for further inquiry, clinical relevance and the limitations of the study. A summary of findings and sample representativeness is presented first.

6.2 Summary of the main findings

The main aim of this study was to examine whether maternal self-reported measures of anxiety, depression and other psychosocial measures in late pregnancy would predict poor mother-infant bonding at six weeks post birth.

An inverse association was found between maternal fetal bonding and mother-infant bonding at one and six weeks postpartum, and there was an independent association between risk of maternal antenatal and postnatal depression as measured using the EPDS and impaired mother to infant bonding at six weeks postnatal. The use of epidural analgesia during labour and birth was associated with poor mother to infant bonding at six weeks postnatal, with need for further exploration of this finding. No evidence was found in this study that women who had a high risk pregnancy had worse mother to infant bonding postnatally. The findings of the pilot study showed no association between maternal salivary cortisol measured in either pregnancy and postnatal with mother-infant bonding score at first or six weeks postnatal. However, a significant association was

found with evening antenatal, alpha amylase and mother-infant bonding at six weeks postnatal.

6.3 Mother-infant bonding six weeks postnatal

The current study investigated the prevalence rate of impaired mother to infant bonding and the prevalence of antenatal and postnatal depressive symptoms in the population studied. The prevalence of impaired mother to infant bonding in a perinatal population has been estimated in previous studies to be between 4% and 12 %, (Taylor et al., 2005, Bienfait et al., 2011, O'Higgins et al., 2013).

In the current study, a prevalence rate of 21% was found at six weeks postpartum, much higher than rates reported previously using the same questionnaire 9%, (Taylor et al., 2005), 12%, (Bienfait et al., 2011). The rate was also higher than in previous studies which used The Postpartum Bonding Questionnaire (Edhborg et al., 2005, Reck et al., 2006, Edhborg et al., 2011) . The reason for the higher rate in the current cohort is likely to be due to the use of lower threshold of ≥ 2 on MIBS used in the current study compared to ≥ 3 in (Taylor et al., 2005) to classify women with impaired mother-infant bonding and differences in range of timing of administration. The present study assessed mother-infant bonding at six weeks postnatal while (Taylor et al., 2005) reported prevalence rate at twelve weeks postnatal. Nevertheless, the higher rate identified should be considered further.

6.3.1 Maternal antenatal and postnatal anxiety

The prevalence estimates for anxiety symptom during pregnancy vary widely in previous studies ranging from 7% to 39 % reflecting differences in population sampling, timing of assessment and measurement tools (interview or self-reported (Sutter-Dallay et al., 2004, Bastani et al., 2005, Adewuya et al., 2006, Borri et al., 2008, Uguz et al., 2010, Goodman et al., 2014, Somerville et al., 2014). Several studies also reported that rates of anxiety may be higher during pregnancy compared to postnatal period (Heron et al., 2004, Lee et al., 2007, Goodman and Tyer-Viola, 2010).

The current study found that just over a third of women exceeded previously defined cut-off points of 40 or more on the Spielberger State anxiety and just under a third on Spielberger Trait anxiety in pregnancy, while 23% women scored 40 or more on the Spielberger State anxiety and 29% on the Trait anxiety at six weeks postnatal. This was similar to Grant et al. (2008) who reported a rate of 33% in STAI- State and Trait anxiety during pregnancy and 26% during the postnatal period using the same measure.

6.3.2 Maternal antenatal and postnatal depression

The increased risk of maternal depression during the perinatal period is well documented with an estimated prevalence rate of 9% to 13% during the antenatal period (Gavin et al., 2005, Melville et al., 2010, Milgrom and Gemmill, 2014) and 10% to 19% during the postnatal period (Dennis and Dowswell, 2013, Gaillard et al., 2013, O'Hara and McCabe, 2013). The estimated prevalence of probable depression in the current study using a threshold

EPDS \geq 13 was 11% in late pregnancy and 12% at six weeks postpartum, similar to that reported in previous studies. Nevertheless the difficulty of comparing estimated prevalence of perinatal depression has been highlighted in (Gaynes et al., 2005, Banti et al., 2011) due to the variations in population, timing of assessment and the criteria used by previous researchers in the assessment and diagnosis of depression.

Although exploring the co-morbidity of antenatal and postnatal depressive symptoms was beyond the aims of this thesis, previous studies have suggested that antenatal depressive symptoms are the most common predictor of postnatal depression (Heron J, 2004, Leigh and Milgrom, 2008, Banti et al., 2011, Gaillard et al., 2014). In the current study, 9 (27%) out of 33 women who scored above the threshold for probable depression during the antenatal period also scored above the threshold at six weeks postnatal.

6.4 Factors associated with poor mother-infant bonding (MIB) six weeks postnatal

The primary aim of this study was to investigate antenatal predictors of impaired mother-infant bonding at six weeks postpartum. These factors included maternal socio-demographic and obstetric characteristics, social support, maternal fetal bonding, anxiety, stress, depression and maternal personality traits as measured using validated scales during pregnancy.

6.4.1 Socio-demographic factors

Evidence of an association between a woman's socio-demographic characteristics and impaired mother-to-infant bonding is unclear with inconsistent findings reported in previous studies (Edhborg et al., 2011, Bicking Kinsey et al., 2014). In the current study no association was found between bonding outcomes and socio-demographic variables of interest, including maternal age, level of education, employment and marital status. The lack of association supports findings of some earlier studies (Moehler et al., 2006, Figueiredo et al., 2009, Edhborg et al., 2011), but contrasts with others (Reck et al., 2006, van Bussel et al., 2010b, Bicking Kinsey et al., 2014). It is likely that differences in the population, timing of the administration of questionnaires and instruments used to assess mother-to-infant bonding account for these inconsistencies. For example, the current study supports findings of Figueiredo and Costa, 2009 who also used the MIBS (Taylor et al., 2005) but not findings of Bicking Kinsey et al (2014) who used the Postpartum Bonding Questionnaire (Brockington et al., 2001). Another plausible reason is the small sample size, with a small number of participants reaching the threshold of probable poor bonding in each socio demographic category. This could have resulted in lack of power to reach statistical significance.

6.4.2 Social support

Maternal social environment and support has been proposed as a positive factor in promoting mother-infant bonding, because it enables mothers to be attentive and responsive to their infants (Kennell and McGrath, 2005, Bicking Kinsey and Hupcey, 2013), an aspect also explored in the current study.

Information on the women's living arrangements was used as an indicator of their social support, but findings indicated that this was neither a confounder nor a mediator of mother-infant bonding in the population studied. This finding contrasts with other studies that examined this with regards to partner support with infant care (Bicking Kinsey et al., 2014).

The lack of an association between maternal support and infant bonding could be explained by how it was assessed in the current study. An assumption was made that women living with their husband, partner or relatives would have some level of support available to them, although in reality this may not have been the case. Bicking Kinsey et al. (2014) measured partner support with the MOS Social Support Survey (Sherbourne and Stewart, 1991) and a 6-item scale developed by the study investigators which included questions such as "In terms of your husband or partner and the new baby, how much of the time does your partner take care of the baby?; and how much of the time is your partner interested in the baby? Another possible explanation for the contrasting findings may relate to the potential that women who did not have a partner or support from other individuals were more emotionally available to focus and develop bonds with their infant as the primary relationship in their lives, which incidentally was also raised as a possibility (Bicking Kinsey et al., 2014).

6.4.3 Maternal emotional health

Another objective of the current study was to explore if maternal symptoms of anxiety, stress and depression during pregnancy predicted poor mother-infant bonding at six weeks postpartum and test for a potential association between

postnatal psychometric measures of anxiety, depression and mother-infant bonding.

There was an association between maternal depressive symptoms during pregnancy and impaired postnatal mother to infant bonding, independent of symptoms of postnatal depression. Overall, women with high depressive symptoms (EPDS \geq 13), but not women who had high anxiety scores as measured using the STAI-State & Trait anxiety in pregnancy reported lower maternal bonding scores six weeks postpartum. This suggests that maternal risk of antenatal depression but not anxiety predict poor mother to infant bonding, a finding which contrast with earlier studies which found the opposite (Kokubu et al., 2012) or no association (Pearce and Ayers, 2005). The main difference is that many previous studies used the Hospital Anxiety and Depression Scale (HADS); (Zigmond and Snaith, 1983) to screen for women at risk of antenatal depression, whereas the EPDS (Cox et al., 1987) was used in the current study.

Current study findings are supported by a recent Japanese study which used similar measures of psychological health and bonding (EPDS and MIBS) and found a significant correlation between maternal depressive symptoms and mother to infant bonding (Ohoka et al., 2014). Similarly, (Perry et al., 2011) found maternal antenatal depression predicted maternal infant attachment at six weeks postnatal assessed using the Maternal Postnatal Attachment scale (Condon and Corkindale, 1998).

6.4.3.1 Postnatal depression

Many previous studies have suggested that the strongest evidence of an association between maternal emotional health and impaired mother to infant bonding is found among women who have highest risk of postnatal depression (Edhborg et al., 2005, Taylor et al., 2005, Moehler et al., 2006, Figueiredo et al., 2009, van Bussel et al., Edhborg et al., 2011, Kokubu et al., 2012, Yoshida et al., 2012, Muzik et al., 2013, Bicking Kinsey et al., 2014, Sockol et al., 2014). The current study findings contribute to this body of evidence. A postnatal EPDS score ≥ 13 , indicative of risk of depression was associated with high MIBS ≥ 2 indicative of impaired maternal bonding.

However, some caution is needed with respect to use of these findings, as a number of women with high EPDS scores at both time points had scores indicative of good maternal bonding and conversely, some women with EPDS score ≤ 13 had MIBS ≥ 2 , indicative of poor maternal bonding. This provides further evidence to suggest that a lack of maternal feelings towards the infant is not only an inherent part of maternal postpartum depressive syndrome, but is likely to be a specific phenomenon on its own (Brockington, 1996, Righetti-Veltema et al., 2003, van Bussel et al., 2010b, Yoshida et al., 2012).

6.4.3.2 Maternal anxiety

Women in this study with a high level of anxiety during pregnancy or in the postnatal period as measured using the Spielberger State-Trait Anxiety Inventory had significantly lower bonding scores than those with low anxiety at both time points, a finding consistent with other studies (Kokubu et al., 2012,

Tietz et al., 2014). However, when combined with maternal risk of depression in further analysis, only maternal depressive symptoms remained significant. This could be due to possible high co-morbidity of anxiety and depressive symptoms as often reported in other studies (Field et al., 2003, Pearce and Ayers, 2005, Klein Hofmeijer-Sevink et al., 2012, Kuo et al., 2014).

6.4.3.3 Maternal stress

No association was found in this study between maternal antenatal or postnatal stress and mother-infant bonding outcomes in contrast to the study by (Bicking Kinsey et al., 2014), likely to be due to the different scales used. For example Bicking Kinsey et al. (2014) used the Psychosocial Hassles Scale (Misra et al., 2001) an 11-item scale which measures maternal perceived stress from no stress to severe stress while the current study used the Stressful Life Event Scale which assessed maternal stress by number of stressful life events. It is possible that the Stressful Life Event Scale may not be an appropriate scale to measure maternal stress because participants in the cohort may not have experienced a recent stressful life event and/or because the scale was unable to capture maternal stress specifically related to pregnancy. This explanation would support Lobel et al. (2008) who suggested that counting the number of life events that occur during pregnancy may not disclose what women are anxious about or whether they experience life events as stressful.

Measurement of pregnancy –specific stress may be more reliable than general or non-specific measures of stress because the pregnancy specific stress scale includes specific reference to pregnancy or birth which improves accurate recall and reporting of stress (Lobel et al., 2008). Alderdice et al. (2012), argues that

studies that disregard pregnancy-specific stress may underestimate the level and extent of stress that women experience during pregnancy.

6.4.4 Maternal fetal bonding

Maternal fetal bonding, as assessed in this study with the Maternal Antenatal Attachment Scale (Condon, 1993) was significantly correlated with the mother-infant bonding score at one and six weeks postnatal after adjusting for maternal depressive symptoms during and after pregnancy. The higher the maternal antenatal fetal bonding score ('good bonding'), the lower the maternal infant bonding score (also indicating 'good bonding'). This supports the early antenatal development of mother-infant bonding reported previously (Muller, 1996, Condon and Corkindale, 1997, Brandon et al., 2009, Figueiredo and Costa, 2009, van Bussel et al., 2010b). As well as in adolescent mothers (Cremona, 2008).

Despite this finding, some women in the current study with a good fetal bonding score had poor mother infant bonding scores postnatally supporting (Sjögren et al., 2004), who postulated that high maternal fetal attachment scores did not necessarily predict a healthier mother-child relationship. This could be due to the complexity of the maternal fetal relationship and individual differences in the way women conceptualise their relationship with their unborn child (Alhusen et al., 2013, Walsh et al., 2013).

With reference to maternal antenatal bonding and maternal emotional health, women in this study with higher depressive and anxiety symptoms during and after pregnancy reported lower feeling towards their fetus in late pregnancy, in

line with other studies which have examined this (Hart and McMahon, 2006, van Bussel et al., 2010a, Maas et al., 2013) . Nevertheless only maternal depressive symptoms during pregnancy remained significantly associated on further analysis, highlighting the importance of taking all potential factors into account. In contrast, no evidence was found in the current study that women who had more perceived stress during pregnancy had poorer maternal fetal bonding.

6.4.5 Mode of birth and neonatal complications

Although there are suggestions that a negative birth experience particularly as a consequence of an operative or traumatic birth can impact on mother-infant bonding (Madrid et al., 2006, Giustardi et al., 2011, van Reenen and van Rensburg, 2013, Sockol et al., 2014), there was no difference in maternal-infant bonding outcomes by mode of birth. It is important to note that a previous study which did report an association was a qualitative study (Madrid et al., 2006), suggesting that some aspects of the birth experience are too sensitive to be measured quantitatively. In addition, no association was found between mother-infant bonding status, birth and neonatal complications in contrast to (Figueiredo et al., 2009, Bicking Kinsey et al., 2014), who found that mothers of infants with neonatal complications had decreased bonding. However as birth and neonatal complications were very low in the current study, findings should be interpreted with caution.

6.4.6 Labour and birth interventions

Labour pain relief in particular epidural analgesia has previously been reported as having a negative impact on mother-infant bonding (Figueiredo et al., 2009). There were no significant association with labour and birth variables in this study, other than for pain relief in labour. A highly significant correlation was found between epidural analgesia and mother-infant bonding, which remained significant after controlling for all other factors. It is difficult to explain this association. Studies that referred to the negative effect of epidural analgesia on maternal bonding appear to have been more focused on maternal infant interaction rather than maternal bonding (Murray et al., 1981, Sepkoski et al., 1992). In contrast, there are extensive personal views and comments on the negative effect of epidural analgesia on maternal bonding on user websites (Theadeutemother, 2011, Kresser, 2014) but no primary studies were identified by the researcher.

Several reasons could be postulated for this finding, all of which would require further consideration based on much larger studies. It could be a chance finding given the high proportion of women in the study that had an epidural or from a physiological perspective, linked to the negative effect of epidural analgesia on maternal oxytocin. Epidural analgesia has been associated with a high use of synthetic oxytocin in labour, which may decrease women's oxytocin regulation (Bell et al., 2014, Olza-Fernández et al., 2014), which has been associated with maternal bonding (Feldman et al., 2007, Galbally et al., 2011, Giustardi et al., 2011, Kim et al., 2013).

Another plausible explanation could be that the association with poor mother-infant bonding may be an indirect relationship or a proxy for poor maternal experience in labour and childbirth. Epidural use has been associated with prolonged labour, instrumental delivery and loss of control in labour and dissatisfaction with the birth experience (Thorp and Breedlove, 1996, Waldenström et al., 2004, Buckley, 2007) which is associated with impaired maternal bonding (Bailham and Joseph, 2003, Madrid et al., 2006).

While epidural analgesia may not have longer-term impacts on health and well-being of most women, findings nevertheless suggest that for some, this intervention could lead to difficulty in their bonding with their infants. Further larger studies are needed to explore this in detail taking all potential confounding factors into account.

It is important to emphasise that combining reasons for epidural analgesia in one group for purposes of analysis could have affected this finding. For instance, women who had epidural analgesia for elective caesarean section may be different from women who had emergency caesarean section, and different again from women who had vaginal birth. Alternative methods of analysis whereby reasons for epidural analgesia are separated and categorised in different groups may have resulted in a different outcome.

6.4.7 Infant feeding

Breastfeeding is often assumed to have a positive effect on maternal-infant bonding, however, evidence to support this assumption is limited and the few studies which have tested this hypothesis have reported contradictory results (Arora et al., 2000, Else-Quest et al., 2003, Jansen et al., 2008, Hahn-Holbrook

et al., 2013). In the current study, no significant association was found between the mother-infant bonding scores of women who breastfed and those who bottle-fed their infants at six weeks post birth. This does not support the suggestion that oxytocin release during breastfeeding facilitates maternal bonding (Kennell and Klaus, 1998) but does provide support for (Bicking Kinsey et al., 2014), who found a lack of association between breastfeeding at one month postpartum and mother-infant bonding. It is also consistent with a breastfeeding and mother-infant relationship review conducted by Jansen et al. (2008) which found a lack of evidence to support a relationship between breastfeeding and mother-infant relationship.

A likely explanation for the finding in the current study is that maternal choice of infant feeding method is complex and associated with a range of other factors, e.g. maternal socioeconomic status, age, educational level, family and social influence (Andrew and Harvey, 2011, Cabieses et al., 2014). Women's emotional feelings towards their infants are unlikely to be determined by their method of feeding if women are happy with their decision about this.

6.5 High risk pregnancy and mother infant bonding

A high risk pregnancy has been associated with increased risk of maternal stress, anxiety (Maloni et al., 2005, Thiagayson et al., 2013, Morrison et al., 2014) and depressive symptoms during pregnancy (Brandon et al., 2008, King et al., 2010, Juhas et al., 2014).

The second objective of the study presented in this thesis was to assess if a high risk pregnancy would affect mother-infant bonding postnatally based on the assumption that high maternal stress, anxiety and depressive symptoms are associated with poor bonding. The study tested this hypothesis by assessing differences in mother-infant bonding status and other psychological outcomes between women with high risk and low risk pregnancies.

Socio-demographic characteristics were similar between the two groups, although there was a higher proportion of a woman of Asian origin in the high risk group. Findings failed to support the hypothesis. Having a high risk pregnancy in this study population did not affect mother-to-infant bonding at six weeks postnatally. Furthermore, there was no significant difference in maternal fetal bonding scores during pregnancy and high or low risk pregnancy.

To this researcher's knowledge, this is the first study to compare mother-infant bonding status in high and low risk pregnancies. Although (Brandon et al., 2008) measured maternal fetal attachment in their study of women at high obstetric risk, they did not compare maternal fetal bonding but rather examined the association between the severity of obstetric risk and reported maternal fetal attachment. Moreover, their study found no significant relationship between the

severity of obstetric risk and maternal fetal attachment, similar to the current study finding.

With regards to other psychological outcomes, there was a highly significant difference in symptoms of antenatal anxiety and depression by high and low risk pregnancy. This concurs with previous UK research, which found significantly higher depression and anxiety scores in high risk pregnant women (King et al., 2010). The current study findings are also consistent with studies from Singapore (Thiagayson et al., 2013), the USA (Brandon et al., 2008) and France (Adouard et al., 2005), which all found significantly higher antenatal depressive symptoms in women with high risk pregnancy.

The observation that women with a high risk pregnancy are more anxious during pregnancy than low risk women, but non-significant differences in their antenatal and postnatal bonding scores is most likely due to women not unexpectedly being more anxious about the welfare of their unborn baby, described previously as a predominant feature of the maternal experience of this cohort (Maloni et al., 2002). This is an important finding for women with high risk pregnancy who may be concerned that they might not be able to bond with their infant. The current study findings suggest these women could be reassured about the longer-term impacts on their relationship with their infant.

6.5.1 Summary

In summary, the study hypothesis that “maternal anxiety, stress, depression and poor fetal bonding during late pregnancy are related to early mother-infant bonding problems six weeks postnatal” was partially supported. Findings showed that maternal fetal bonding and antenatal depression were associated with impaired mother-infant bonding after taking account of a range of relevant postnatal factors that could influence this. Although use of epidural analgesia during labour and delivery appeared to be associated with maternal impaired bonding in the current study, there is insufficient supporting evidence from the literature to support this association and further research is needed.

The second hypothesis that having a high risk pregnancy would affect mother-infant bonding postnatal was not supported by the evidence in the current study.

6.6 Pilot study

The pilot study was completed on a subset of participants who provided saliva samples during late pregnancy and six weeks postnatally. It was undertaken as an opportunity to use the same cohort of women to assess if using biological measures of stress (salivary alpha-amylase and cortisol) during pregnancy could identify women who may develop early mother-infant bonding problems postnatally. Findings could be used to inform a larger study if initial results looked promising in terms of recruitment and adherence of women to the study protocols and initial analysis of results.

The main finding of the pilot study related to the distinct diurnal patterns of cortisol and alpha-amylase, which was consistent with previous studies (Nater et al., 2007, Kivlighan et al., 2008). More specifically, the results confirmed that maternal salivary cortisol levels changed markedly between the antenatal and postnatal period and that unlike cortisol, salivary alpha-amylase did not change during this period. No association was found between maternal levels of cortisol or alpha-amylase during pregnancy or the postnatal period and no association with mother to infant bonding postnatally. Conversely, a reverse relationship to that hypothesised was found, as raised maternal salivary alpha-amylase was associated with poor mother-to-infant bonding six weeks postnatal in this population.

6.6.1 Diurnal profile

Participants in the pilot study displayed a normal salivary cortisol diurnal profile. That is, a rise in levels from waking, peaking at 30 minutes post waking, followed by declining levels throughout the rest of the day (Kivlighan et al., 2008). The salivary alpha-amylase pattern mirrored that of cortisol with a decline 30 minutes post-waking, followed by increasing levels throughout the day. This outcome was consistent with other studies that found similar diurnal profiles in pregnant (Giesbrecht et al., 2013), and in non-pregnant women (Nierop et al., 2006, O'Donnell et al., 2009a, Ali and Pruessner, 2012, Pilgrim et al., 2014).

6.6.2 Changes in maternal cortisol and alpha amylase levels

Consistent with the literature, the results showed a significant change in cortisol levels over the perinatal period, with a decrease between the antenatal and postnatal measures (Mastorakos and Ilias, 2003, Kammerer et al., 2006, Field and Diego, 2008). This change is thought to reflect the physiological modifications of the HPA axis over the perinatal period, from hyper-activation during pregnancy and a decline to pre pregnancy state during the postnatal period (Duthie and Reynolds, 2013).

With regards to maternal salivary alpha-amylase, the current study found no significant changes in the levels between the antenatal and postnatal periods. This finding is novel as the diurnal course of salivary alpha-amylase from pregnancy to the postnatal period has not been described previously. Studies of pregnancy-related changes in alpha amylase are limited with those identified which investigated salivary alpha-amylase during pregnancy reporting conflicting results. (Salvolini et al., 1998) observed an increase in alpha

amylase activity in the first trimester of pregnancy, followed by a decrease by the time of the birth, whereas others reported that levels are not affected by pregnancy gestation (Laine et al., 1988, D'Alessandro et al., 1989).

A more recent study that investigated the diurnal pattern of salivary alpha amylase secretion during pregnancy collected salivary samples over three days from 96 pregnant women who were between six and 37 weeks gestation and reported no significant correlation with gestational age (Giesbrecht et al., 2013). In contrast, a Brazilian study found an increase in salivary alpha-amylase levels during pregnancy (Abrao et al., 2014), however, because this was written in Portuguese, only the abstract was accessed and it was not possible to compare these two studies in detail.

6.6.3 Association between maternal salivary cortisol and antenatal depressive / anxiety symptoms

Associations between mood symptoms and an altered HPA axis (cortisol production) in non-pregnant individuals have been reported in several studies (Burke et al., 2005, Van den Bergh et al., 2008, Hellhammer et al., 2009). The current study examined association between maternal self-reported measures of anxiety, stress and depression with maternal salivary cortisol and alpha amylase.

The pilot study found no association between maternal self-reported measures of anxiety or depression with maternal salivary cortisol. Similarly, there was no difference in the cortisol diurnal pattern or the cortisol awakening response (CAR), (a measure of HPA-axis reactivity) between women with high maternal

stress and depressive symptoms during pregnancy and those without, consistent with some studies with similar findings, (Davis and Sandman, 2010, King et al., 2010, Hellgren et al., 2013). However, the finding is in contrast to other studies which reported differences between the two groups (Field et al., 2004, Obel et al., 2005, Suglia et al., 2010, Rothenberger et al., 2011, Voegtline et al., 2013, O'Connor et al., 2014).

Inconsistencies in findings across studies are somewhat difficult to reconcile given that measures of depression and measurement of maternal cortisol diurnal profile overlap substantially. For example, Field et al. (2004) analysed urine rather than saliva to determine cortisol levels. O'Connor et al. (2014) oversampled with high racially/ethnically diverse sample of women from a high psychosocial risk group. Moreover, the association in O'Connor et al's (2014) study was found using a clinical diagnosis of depression based on clinical interview rather than self-rating questionnaire. Voegtline et al. (2013) relied on cortisol samples collected in mid-afternoon (single assessment of cortisol); meaning that their study failed to use the optimal index of multiple measurements reflective of the cortisol awakening response or diurnal secretory pattern (Harville et al., 2007). In the same study (Voegtline et al. 2013), depressive symptoms were measured using The Centre for Epidemiological Survey Depression Scale (CES-D) (Radloff, 1977) and not the EPDS. Rothenberger et al. (2011) used a perceived stress questionnaire and only found the association in the first and second trimester of pregnancy.

6.6.4 Salivary cortisol and postnatal stress and depressive symptoms

There was no correlation between maternal salivary cortisol during the postnatal period and self-reported measures of stress and depressive symptoms in this study. However, comparison of the cortisol diurnal pattern showed that postnatal women with symptoms of depression exhibited a different pattern from those without. Women with higher EPDS scores (≥ 13), had a significantly lower morning rise compared to women with lower scores ($EPDS < 13$) which concurs with (Taylor et al., 2009). Groer and Morgan (2007) also found lower salivary cortisol in depressed postnatal women, which in part supports the model proposing that depressive symptoms are associated with the hypo responsive HPA axis in the postpartum period (Glynn et al., 2013).

6.6.5 Salivary cortisol and maternal anxiety measures

There were no differences in cortisol levels between women with STAI- State & Trait anxiety score ≤ 40 and ≥ 40 during pregnancy. (Petraglia et al., 2001, Harville et al., 2009) also found no correlation between reported psychosocial measures and cortisol in pregnant women. However, this contrasts with other studies (Kivlighan et al., 2008, Giesbrecht et al., 2012, Kane et al., 2014). Variations in timing, method and instrument used could explain these contradicting findings. For example, the current study measured maternal cortisol at 36 weeks gestation and assessed maternal anxiety with STAI-State & Trait anxiety while Kane et al (2014), found association with saliva cortisol at 30 weeks gestation and maternal psychosocial anxiety was assessed with a modified Perceived Stress Scale (PSS) (Glynn et al., 2008).

6.6.6 Salivary alpha amylase, stress, anxiety and depression

There is a growing interest in using salivary alpha-amylase as a non-invasive, surrogate marker for sympathetic activities as studies in non-pregnant adults have showed that this increases in states of stress (Nater and Rohleder, 2009).

The results of the current study showed no correlation between maternal anxiety, stress and depressive scores with maternal salivary alpha-amylase values during pregnancy or in the postnatal period. Bosch et al. (2011), proposed that factors such as salivary flow rate, duration and collection material, i.e. use of cotton roll Salivettes, may affect the values of salivary alpha-amylase, introducing measurement error. Furthermore, non-stressful activities, such as smoking, alcohol intake and food intake could alter enzyme levels (Stegmann, 2011), a range of factors not adjusted for in the current study.

Women with high EPDS scores (≥ 13) and women with high anxiety (State-Trait Anxiety Inventory score ≥ 40) during pregnancy had lower evening alpha amylase, although this was not statistically significant. No previous studies were identified which had studied the relationship between self-reported measures of anxiety and depression and salivary alpha-amylase in the perinatal period. However, as the sample of women with high EPDS scores who provided saliva samples was small ($n=9$) findings must be treated with caution. Nevertheless, this provides some support that changes in salivary alpha-amylase reflect adrenergic dysregulation which has been associated with anxiety related disorder in the general adult population (Schumacher et al., 2013).

6.6.7 Salivary cortisol, alpha-amylase and mother-infant bonding

There was no association between cortisol and mother-to-infant bonding in the antenatal or postnatal period, consistent with the study by (Figueiredo et al., 2009). However, this contrasts with findings of previous studies which found increased antenatal and postnatal cortisol levels in women who were more emotionally involved with their infants (Fleming and Corter, 1988; Fleming et al., 1997; Giardino et al. 2008). It is important to note that this did not imply better bonding.

With regards to maternal salivary alpha-amylase and mother-infant bonding, there was a significant correlation between maternal salivary alpha-amylase collected at eight hours post waking during the antenatal period and mother-infant bonding at six weeks postnatally. However, this finding should be treated with caution as the numbers were small, and the association was only found only at one collection time. Nevertheless, these pilot study findings could be used as a basis for future work. This was the first study to investigate an association between maternal salivary alpha-amylase levels in human pregnancy with early mother-to-infant bonding. Some animal studies have suggested that noradrenalin, which alpha-amylase is thought to reflect (Chatterton et al., 2006), plays a significant role in maternal bonding (Moffat et al., 1993).

6.6.8 Feasibility of larger study from pilot study

A second objective of the pilot study was to ‘test’ the potential for conducting a future larger study of use of maternal salivary samples to predict early mother-infant bonding problems. Pilot study recruitment, response rates and quality of saliva sample collected were important issues to consider.

The National Institute for Health Research NIHR (2011) defined pilot studies “as a mini version of the main study with the aim of assessing if the process of the main study will run smoothly”. The main problems identified from the current pilot study included difficulty recruiting and retaining participants, compliance with returning samples as requested and poor quality of saliva samples returned. The conclusion drawn is that although there were important pragmatic issues which would need to be considered, the finding of a possible association between maternal salivary alpha-amylase and mother infant bonding is important, and should warrant a larger study to confirm the finding. Modifications would need to be made to the study protocol to support compliance, and future studies could explore the use of electronic monitoring devices for saliva sampling to support compliance (Broderick et al., 2004, Entringer et al., 2009, Moeller et al., 2014). It is also possible that reducing the frequency of saliva collection from four times a day to twice a day could improve the retention rate.

6.6.8.1 Summary

Findings from the pilot study suggest that raised maternal salivary cortisol in late pregnancy or postnatal period is not related to poor mother-infant bonding early weeks postpartum, but raised evening maternal salivary alpha-amylase during pregnancy could infer better mother-infant bonding postnatal. Due to the lack of statistical power, this requires further investigation with careful consideration of study processes with reference to the previous paragraph.

6.6.9 Contribution to knowledge

The current study used a prospective longitudinal method to identify potential antenatal 'roots' of maternal-infant bonding. The findings from this thesis have contributed to the evidence and add to the extant literature in the following ways:

- *It supports antenatal root of impaired mother-infant bonding*
- *Impaired mother-infant bonding is linked to maternal mental health*
- *Impaired mother-infant bonding can be regarded a specific phenomenon and not simply a feature of maternal anxiety or depression*
- *Maternal antenatal anxiety and depression is associated with maternal postnatal depression*

This study was the first to compare mother-infant bonding outcomes among women with high and low risk pregnancies. The finding that the former was not associated with impaired mother-infant bonding is novel and can be used to reassure women who have a high risk pregnancy who may be worried that they may not be able to bond with their infants. Larger studies, involving a range of

data collection approaches are now needed to confirm current study findings and explore women's feelings about their pregnancy and relationship with the foetus in greater detail.

An unexpected finding was a potential association with use of epidural analgesia during labour and delivery on mother-infant bonding in the early weeks postnatal, but further studies are needed to confirm as it could have been a spurious finding for the reasons suggested earlier.

With regards to salivary biomarkers of stress during the perinatal period, the current study has contributed to the literature in several ways. It provides further understanding of the range of levels of salivary alpha-amylase and cortisol in pregnancy and the postnatal period and is the first study to examine the diurnal profile of salivary biomarkers from late pregnancy through to the postnatal period.

The finding that unlike salivary cortisol, the diurnal profile of maternal salivary alpha-amylase is stable and did not change across the postnatal period is novel. If this protein enzyme is confirmed to be a biomarker of stress regulation, it may provide a better assessment tool due to its stability.

Finally, high antenatal evening alpha amylase levels correlated with good mother-infant bonding and if confirmed, salivary alpha-amylase could potentially be used to identify mothers at risk of bonding failure during pregnancy. A larger study would need to be done before; this can be recommended for practice.

6.6.10 Study limitations

The study results were based on a population of women attending for maternity care in a large tertiary hospital in a diverse area of West London. Most women receive their antenatal care at the hospital, although women classed as vulnerable due to adverse social or other circumstances are assessed at home contacts by the one-to-one midwifery teams. Several efforts were made to recruit women classed as vulnerable as circumstances such as low level of education, and poor financial situations are associated with poor maternal bonding (Figueiredo et al., 2009, Bicking Kinsey et al., 2014). Moreover, poverty, adverse social situation including partner's violence and poor support are factors strongly associated with maternal depressive symptoms (Lancaster et al., 2010, Edhborg et al., 2011, Prady et al., 2013) which could indirectly affect mother-to infant bonding. However, the majority of women recruited from this group did not return study questionnaires despite being sent reminders by text, phone calls and letters. It is possible that the rate of impaired mother-infant bonding and postnatal mental health issues were underestimated as a result of poor representation of potentially high risk groups of women.

Around 600 women were approached to take part in the study but due to resource limitations, the study excluded women unable to speak English. Approximately, 15% of eligible women declined to take part for different reasons. Although the number of women who declined was small, it is possible that the study sample may not be representative of the population attending the maternity unit, thereby affecting the generalizability of the study finding.

The study sample was also less representative of the local population of women. Study respondents were older, more likely to be primiparous, of white ethnicity and higher educational attainment compared to study non-respondents. Nevertheless, participants were representative of the population of women attending the antenatal clinic of the study hospital and consistent with study populations recruited from the same site in previous studies (Bergman et al., 2007, King et al., 2010, O'Higgins et al., 2013).

There was a poor representation of ethnic minority groups in the study sample, with 65% of the women of White ethnicity, 11% Asian, 7% Black and 14% other ethnic group. However, this is not unique to the current study as difficulties engaging participants from different ethnicities in research have been reported previously (Woodall et al., 2010, Barnett et al., 2012, Henderson and Redshaw, 2013). Consequently, it is difficult to extrapolate the findings of this study to a population with greater ethnic diversity.

6.6.10.1 Limitation of scales and measures used

Data were collected using self-administered questionnaires. While scales used were carefully selected to meet study aims and objectives, some were not developed for perinatal populations and consequently cut-off thresholds were not helpful in answering some study questions. For example, the Standardised Assessment of Personality-abbreviated Scale (SAPAS) was developed to screen for personality disorder in patients with a range of psychiatric problems. A score of three and above is considered a probable personality disorder (Moran et al., 2003). Around 25% of participants in the current study had a

score of three and above which raises the question as to whether this scale was appropriate for assessing personality disorder in a perinatal population.

The Stressful Life Event Scale (Bergman et al., 2007) was used to assess maternal stress during pregnancy and postnatal period, however it is possible that the scale used in the current study was not the most appropriate in assessing maternal stress in the current cohort for reasons described earlier.

(Lobel et al., 2008). Conversely, the Mother Infant Bonding Scale (MIBS) was used as an outcome measure and a threshold score of 2 or more selected to identify women who probably had impaired mother-infant bonding. Although this threshold has been validated through clinical interviews in the first week postnatal (Bienfait et al., 2011), and used in samples of women with low levels of literacy (van Bussel et al., 2010b), using this threshold in highly educated women at six weeks postnatal (as was the case in the current study) may have resulted in an overestimation of women with impaired mother-infant bonding.

Another study limitation was the use of participants living arrangements as an indicator of social support. Living with another adult may be a better indicator of immediate social network, or 'family support' but may not imply social support. The study would have benefited if standardised measures of social support such as Norbeck Social Support Questionnaire(NSSQ) (Norbeck, 1983); Maternity Social Support Scale (MSSS) (Webster et al., 2000) or Social Support Questionnaire (SSQ) (Sarason et al., 1987), had been used. The lack of association between mother–infant bonding in the current study may not be a true reflection of what is happening in reality.

6.6.10.2 Reliability of scales

Reliability of all scales used was tested by initially examining their internal consistency. Cronbach's Alpha values indicated good reliability for almost all scales used except for the SAPAS which had low internal consistency ($\alpha=0.46$ and 0.48). Although the results provided the first validation for its use with a pregnant population, measuring maternal personality in perinatal women using the same scale will require further investigation through clinical interviews to establish the threshold for personality disorder in a perinatal population.

6.6.10.3 Reporting bias

Although use of a prospective longitudinal study design was appropriate to answer the study questions, outcome data were taken from responses to self-administered questionnaires rather than formal diagnostic interviews. Reporting bias is difficult to prevent or estimate as respondents are likely to skip some questions, and/or misinterpret them in the absence of the researcher who would otherwise be able to clarify any misunderstanding (Krohn et al., 2013, Polit and Beck, 2013). The skipping of questions was evident as some questionnaires were only partially completed when returned. In addition, some women with a low bonding score indicating good bonding may have answered questions to reflect social acceptability due to the sensitive nature of impaired mother-infant bonding. Moreover, the coexistence of maternal depression may have distorted participants' self-reporting of attitudes, such as lack of affectionate feelings towards the infant (Ohoka et al., 2014).

The pilot study relied on maternal self-reporting of saliva sample collection times. Despite provision of comprehensive instructions on how to collect the samples and the scheduled sampling times, some women were unable to comply with these requirements, resulting in samples being discarded due to insufficient volume (Moeller et al., 2014).

6.6.10.4 Sample size

The small sample size resulted in unbalanced groups in some variables. Testing more participants who met the threshold of poor bonding could have potentially increased statistical power to confirm or refute the study's finding especially with maternal demographic and obstetric information where the number of cases in each category was relatively small.

6.7 Implications for policy and practice

Despite the limitations, findings presented in this thesis have a number of potential implications for policy and practice.

6.7.1 Antenatal assessment of impaired mother-infant bonding

With current government policy focusing on early interventions with families as the most effective way of tackling child development, health and well-being (for example the Healthy Child Programme DOH, 2013), there has been increased emphasis on early identification and intervention in order to offer all children the best start in life, commencing in pregnancy or pre-conception (D.O.H, 2013).

Pregnancy and the early postnatal period are opportunistic times for health education due to the frequency of routine contacts with health care providers. The use of a short self-report measure to assess maternal psychological health to aid clinical decision-making has been recognised (Alderdice et al., 2013).

Maternal psychosocial wellbeing assessment during the antenatal period should include assessment or discussion of poor mother-fetal bonding. However there are strong debates as to the benefit of routine screening for perinatal mental health problems due to high false positive results (for example screening for depression using the EPDS) which may lead to misdiagnosis and increased prevalence reporting of the disorder (Matthey, 2010, Austin, 2014). It is also important to consider management a pathway if a 'case' is identified as a consequence of screening.

Nevertheless, assessing or talking to women about maternal fetal bonding during antenatal contacts may facilitate communication between the woman and her midwife about her feelings towards her unborn child. This could be in a form of a simple checklist as used by (Henderson and Redshaw, 2013) where women were asked about their experiences of various health problems in pregnancy could provide valuable information for the midwives about a woman's feelings for her fetus. Referral to specialist services e.g. perinatal psychiatrist could be made as appropriate or it may encourage the women to seek help from health care provider if she needs more support during the postnatal period.

6.7.2 Postnatal care

Presently, interventions to support postnatal bonding following birth include physical contact between a woman and her infant and support for breastfeeding (RCM, 2012, Leyland and Bond, 2014). To further promote mother to infant bonding, midwives should promote not only closer physical proximity of a mother and her new-born, but also women's positive emotional health (Bicking Kinsey and Hupcey, 2013, Mivšek and Zidaric, 2013).

Midwives have an important role in promoting mother-infant bonding during the postnatal period however, due to rapid discharge from hospital, postnatal care in the community has become increasingly important given the potential to contribute to the health and wellbeing of the new mother and her family. In the current system of routine postnatal care, routine midwifery contacts end at around 10-14 days and the postnatal period at 6-8 weeks postnatally (NICE, 2006). There is lack of evidence to support timing and content of postnatal care and little evidence that contacts are tailored to maternal and/or infant need (Bick, 2009, Brodribb et al., 2014).

The results of the current study showed that even women with low risk of maternal depression could develop impaired mother-infant bonding. NICE (2006) already recommends that home contacts should be used as an opportunity to promote mother-infant emotional attachment but does not provide detail of how to achieve this. Nevertheless incorporating some form of assessment for impaired mother-infant bonding as part of woman's overall psychological well-being could enhance early identification of those who may be

at risk of this disorder and promote better continuity of care between members of the primary health care team. Appropriate referral may reduce the duration of the problem and could potentially ameliorate subsequent long term effects of impaired mother-infant bonding on the individual, child and wider society.

Moreover, the adverse effect of maternal depression on mother-infant interaction and child behaviour is well established (Sutter-Dallay et al., 2011, Sellers et al., 2014). Consequently, the link between maternal depression and mother to infant bonding reported in the current study is of clinical relevance and justifies an intensification of efforts to identify and support women most at risk.

6.7.3 Increasing awareness of mother-infant bonding disorder

The study outcomes suggest that awareness of poor maternal fetal bonding and educating clinicians on how to recognise this condition is important. Preventive programmes targeting the mother-infant relationship in pregnancy and first few months of a child's life which includes positive image of baby, music therapy during pregnancy, infant massage and early parenting programmes during the postnatal period could promote better bonding between a woman and her infant (Barlow, 2008, RCM, 2012). As poor mother-infant bonding can also occur in the absence of postnatal depression, (van Bussel et al., 2010b, Brockington, 2011, O'Higgins et al., 2013, Ohoka et al., 2014), awareness of this problem for the clinicians and mothers is important as it will encourage early recognition of the problem and encourage women to seek help if required.

6.7.4 Nested pilot study

Given the demanding nature of saliva sample collection for the nested pilot study especially during the postnatal period, the findings of the pilot study suggest it would not be practical to ask women to incorporate collection of saliva samples four times a day into their daily routines. Hence, physiological assessment of maternal emotional state is not recommended in assessing mother-infant bonding.

6.8 Future research

Poor mother to infant bonding in this study was assessed using a self-report scale with a score of two or more indicating probable risk of poor mother-infant bonding. An important next step would be to determine threshold validity of the MIBS where women who scored ≥ 2 would be followed up with a structured diagnostic interview by a perinatal psychiatrist to confirm clinical relevance of this scale. In addition, further research with a larger sample size and longer follow-up is needed to find out the degree of impaired mother-infant bonding that has an adverse effect on the child. Furthermore, to clarify the risks related to poor mother-to-infant bonding, future studies should include additional information regarding social support, pregnancy specific stress and use of epidural pain relief during labour and birth.

6.9 Conclusion

Mother-infant bonding is a complex concept with many inconsistencies in the way it is currently defined. Despite the fact that the majority of women develop affectionate feelings towards their infants, some have problems with this process. This thesis has explored the antenatal factors associated with impaired mother - infant bonding using maternal feelings and emotions towards the infant as primary indicators of this phenomenon. The results have shown that maternal depressive symptoms during pregnancy and poor fetal bonding negatively impacted on a woman's emotional bonding with her infant as assessed at six weeks postnatally. The current study also investigated the impact of high risk pregnancy on mother-infant bonding which found no association.

As maternal emotional bonding commences during pregnancy in some women, the outcomes of the study highlight the importance of specific awareness for impaired mother-infant bonding and justifies the need for better assessment of maternal emotional and mental health during the perinatal period.

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Appendix 1 STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any pre-specified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias

	Item No	Recommendation
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	<p>(a) Describe all statistical methods, including those used to control for confounding</p> <p>(b) Describe any methods used to examine subgroups and interactions</p> <p>(c) Explain how missing data were addressed</p> <p>(d) <i>Cohort study</i>—If applicable, explain how loss to follow-up was addressed <i>Case-control study</i>—If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i>—If applicable, describe analytical methods taking account of sampling strategy</p> <p>(e) Describe any sensitivity analyses</p>

Results

Participants	13*	<p>(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed</p> <p>(b) Give reasons for non-participation at each stage</p> <p>(c) Consider use of a flow diagram</p>
Descriptive data	14*	<p>(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders</p> <p>(b) Indicate number of participants with missing data for each variable of interest</p> <p>(c) <i>Cohort study</i>—Summarise follow-up time (e.g., average and total amount)</p>
Outcome data	15*	<p><i>Cohort study</i>—Report numbers of outcome events or summary measures over time</p> <p><i>Case-control study</i>—Report numbers in each exposure category, or summary measures of exposure</p> <p><i>Cross-sectional study</i>—Report numbers of outcome events or summary measures</p>

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(b) Report category boundaries when continuous variables were categorized
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.
(von Elm et al., 2007)

CRITICAL APPRAISAL SKILLS PROGRAMME
Making sense of evidence about clinical effectiveness



12 questions to help you make sense of cohort study

General comments

- Three broad issues need to be considered when appraising a cohort study.

Are the results of the study valid?

What are the results?

Will the results help locally?

The 12 questions on the following pages are designed to help you think about these issues systematically.

- The first two questions are screening questions and can be answered quickly. If the answer to those two is "yes", it is worth proceeding with the remaining questions.
- There is a fair degree of overlap between several of the questions.
- You are asked to record a "yes", "no" or "can't tell" to most of the questions.
- A number of italicised hints are given after each question. These are designed to remind you why the question is important. There will not be time in the small groups to answer them all in detail!

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Appendix 3 Study sample size calculation

Prediction & biological correlates of bonding problems in new mothers

Statistical Analysis Plan and Sample Size Calculation

Bernard North
Statistical Advisory Service
Imperial College

Determine whether women who go on to have difficulty bonding with their new infant can be identified antenatally by the use of psychometric rating scale and / or biochemical markers.

Bonding will be assessed by the Mother to Infant Bonding Scale (MIBS) where poor bonding is defined as a score of 3 or more. Depression will be assessed by the Edinburgh Postnatal Depression Scale (EPDS).

Statistical Analysis

Previous published research demonstrates that the questionnaire data is highly skewed to the right.

Correlation between antenatal EPDS and MIBS score can be performed by a non-parametric Spearman rank correlation, but the main statistical test for association will be a Fisher Exact test of presence or absence of depression (depression being a score of 12 or more on the EPDS) and presence of absence of poor bonding (poor bonding is defined as a score of 3 or more on the MIBS)

Mann-Whitney-U will be calculated to test for significant differences of scores on self rating scales.

Sample Size Calculation

If we assume 225 mothers available for study then it is expected that 15% = 34 will be depressed.

If we assume a proportion of 15% of non-depressed mother will have poor bonding and a proportion of 40% of mothers will have poor bonding (odds ratios = 3.7) then we have a power of 90% to detect this difference with a 1 sided Fisher's Exact test with at a significance level of 0.05.

The sample size calculation with performed using the package NCSS PASS (Hintze 2001)

Fisher's Exact Test Power Analysis

Page/Date/Time 1 25/07/2007 17:27:26


Numeric Results for Fisher Exact Test

Null Hypothesis: P1=P2 Alternative Hypothesis: P1>P2

Power	Allocation			P1	P2	Odds Ratio	Alpha	Beta
	N1	N2	Ratio					
0.74424	34	191	0.178	0.40000	0.15000	0.285	0.01000	0.25576
0.89753	34	191	0.178	0.40000	0.15000	0.265	0.05000	0.10247

Hintze J. L. 2001. NCSS User's Guide IV. Number Crunching Statistical Systems Inc., Kaysville, Utah, USA.

Appendix 4 Ethic approval letter

	 National Research Ethics Service Charing Cross Research Ethics Committee Room 4W/12, 4th Floor Charing Cross Hospital Fulham Palace Road London W6 8RF Telephone: 020 8846 7283 Facsimile: 020 8846 7280
--	--

Professor Vivette Glover Professor of Perinatal Psychobiology Imperial College London Institute of Reproductive and Developmental Biology Du Cane Road London W12 0NN	30 October 2007
--	-----------------

Dear Professor Glover

Full title of study:	Prediction and biological correlates of poor mother-infant bonding in new mothers
REC reference number:	07/H0711/97

Thank you for your letter of 12 October 2007, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Ethical review of research sites

The favourable opinion applies to the research sites listed on the attached form.

Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	Version	Date
Application		10 August 2007
Investigator CV		
Protocol		
Covering Letter		07 August 2007
Letter from Sponsor		06 July 2007
Statistician Comments		
Questionnaire: Mother-Infant Bonding Scale		

This Research Ethics Committee is an advisory committee to London Strategic Health Authority
The National Research Ethics Service (NRES) represents the NRES Directorate within
the National Patient Safety Agency and Research Ethics Committees in England

Questionnaire: MAAS		
Questionnaire: EPDS		
Questionnaire: Life Events		
Questionnaire: Spielberger State-Trait		
Questionnaire: Assessment of Personality (SAPAS)		
GP/Consultant Information Sheets	1	
Participant Information Sheet	2	12 October 2007
Participant Consent Form	1	01 May 2007
Response to Request for Further Information		12 October 2007
CV: Catherine Williamson		
CV: Alyx Alison Taylor-Vieira		
Letter from the funder		09 March 2007
Statement of indemnity		13 August 2007

R&D approval

All researchers and research collaborators who will be participating in the research at NHS sites should apply for R&D approval from the relevant care organisation, if they have not yet done so. R&D approval is required, whether or not the study is exempt from SSA. You should advise researchers and local collaborators accordingly.

Guidance on applying for R&D approval is available from
<http://www.rdforum.nhs.uk/rdform.htm>.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Website > After Review

Here you will find links to the following

- Providing feedback. You are invited to give your view of the service that you have received from the National Research Ethics Service on the application procedure. If you wish to make your views known please use the feedback form available on the website
<https://www.nationalres.org.uk/AppForm/Modules/Feedback/EthicalReview.aspx>.
- Progress Reports. Please refer to the attached Standard conditions of approval by Research Ethics Committees.
- Safety Reports. Please refer to the attached Standard conditions of approval by Research Ethics Committees.
- Amendments. Please refer to the attached Standard conditions of approval by Research Ethics Committees.
- End of Study/Project. Please refer to the attached Standard conditions of approval by Research Ethics Committees.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email
referencegroup@nationalres.org.uk.

An advisory committee to London Strategic Health Authority

Appendix 5 Trust approval letter

Imperial College Healthcare **NHS**

NHS Trust

Hammersmith Hospital
Research & Development Office
1st floor, Ham house
Du Cane Rd
London
W12 0HS
P: 020 8383 3329
F: 020 8383 4957
www.imperial.nhs.uk/research

Prof Vivette Glover
Perinatal Psychobiology
Queen Charlottes & Chelsea Hospital
Hammersmith Hospital
Du cane Road
London
W12 ONM

COPY

13th December 2007

Dear Professor Glover,

RE: Trust Approval - Research Governance Registration

Project Title: Prediction and biological correlates of poor mother-infant bonding in new mothers

Our Project Reference: GLOV3024

Ethics Reference: 07/H0711/97


College Reference: cro834

With regard to the above, we are pleased to confirm that your project complies with all necessary research governance registration requirements and is therefore officially recognised and approved.

We wish you every success in the progression of this project. Please note our reference number and use it in all future communications.

If you have any questions or need clarification please contact me or my senior team members Anu Upadhyia (020 8383 4959 anu@nhs.net) or Jo Morgan (020 8383 4952 jo.morgan@imperial.nhs.uk). If you find any errors or can suggest ways to make the process run more smoothly, please let me know.

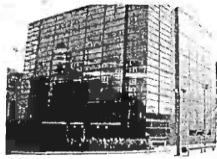
Yours sincerely



Dr Rodney Gale
Director of Research Support

The UK's first Academic Health Science Centre incorporating St Mary's and Hammersmith Hospitals in partnership with Imperial College London

Appendix 6 Research grant letter



INSTITUTE OF OBSTETRICS AND GYNAECOLOGY TRUST

Promoting Better Health for Women and Babies

Wolfson & Weston Research Centre for Family Health
Imperial College London
Hammersmith Hospital
Du Cane Road
London W12 0NN

09 March 2007

Professor V Glover
Division of SORA
1st Floor, IRDB Building
Imperial College London
Hammersmith Hospital
Du Cane Road
London W12 0NN

Dear Vivette

Application for Funding Research – ‘Prediction and biological correlates of bonding problems in new mothers’ - £9,853

I am happy to let you know that at the Institute of Obstetrics and Gynaecology Trust meeting on 7th March 2007 the trustees agreed to support your application for £9,853 for funding research into prediction and biological correlates of bonding problems with new mothers.

The trustees asked me to make it clear that they could only fund this pilot study for a year and after this initial stage is complete you would have to find funding from an external body.

For your information I am enclosing the IOGT terms and conditions under which grants are awarded and request that you name the IOGT as sponsors in any publications regarding this study.

Best wishes
Yours sincerely

Gwen Young
Trust Secretary

Cc Shirley Line

Trustees: Professor Lord Winston (Chairman), Mr DRL Duncan, Professor NM Fisk, Mr DB Jones, Mrs LC Loftus, Mr RA Margara, Professor MG Parker, Professor L Regan, Mr AS Rosenfelder, Secretary: Ms GA Young, Accountant: Mr PJ Clark FCA FBIM
Registered Charity No. 292518

Telephone: 020 7594 2143 Fax: 020 7594 2157 e-mail: g.young@imperial.ac.uk website: www.iogt.org.uk

Appendix 7 Research sponsor letter

**Imperial College
London**

Faculty of Medicine
Imperial College London

G02 Sir Alexander Fleming Building
South Kensington Campus
London, SW7 2AZ
Tel: +44 (0)20 7594 1188 Fax: +44 (0)207 594 1792

gary.roper@imperial.ac.uk
www.imperial.ac.uk/clinicalresearchoffice

Gary Roper
Research Governance Manager

Our ref: cro834

6 July 2007

Professor Vivette Glover
Professor of Perinatal Psychobiology
Institute of Reproductive and Developmental Biology
Imperial College
Hammersmith Campus

Dear Professor Glover,

Re: Prediction and biological correlates of poor mother-infant bonding in new mothers

This is to confirm that the above named research project utilises human participants, their organs, tissue and/or data as defined under the sponsorship requirements of the Research Governance Framework for Health and Social Care 2005, incorporating the Medicines for Human Use (Clinical Trials) Regulations 2004.

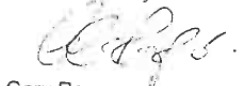
On behalf of Imperial College of Science, Technology and Medicine, we undertake to act as the identified Research Sponsor for this project.

This letter confirms:

- The research proposal has been discussed, assessed and registered with Imperial College Clinical Research Office and provisional sponsor approval granted.
- The Chief Investigator has undergone a process of scientific critique commensurate with the scale of the project.
- Indemnity and insurance arrangements have been put in place to cover the project.
- Resources and support are available to the research team to aid delivery of the research as proposed.
- Management, monitoring and reporting responsibilities for the research have been approved.
- Imperial College will undertake and enforce those sponsor duties set out in the NHS Research Governance Framework for Health and Social Care.

Imperial College Sponsorship is conditional on the project receiving applicable ethical and regulatory approval for all research related aspects of its conduct. A copy of the ethics approval letter **must** be sent to the Research Governance Manager prior to the study commencing. Sponsorship is dependant on obtaining R&D Office approval for all NHS sites where the research is being conducted.

Yours sincerely



Gary Roper
Research Governance Manager
Faculty of Medicine
Imperial College London

Prediction and biological correlates of mother-infant bonding in new mothers. REC. No: 07/H0711/97:

You are invited to take part in a research study

Please take time to read the following information carefully and discuss it with others if you wish. Before you decide whether to take part or not, it is important for you to understand why the research is being done and what it will involve.

What is the purpose of the study?

Pregnancy may cause some women to experience emotional disturbance, for example anxiety or depression. Some mothers find that they have difficulties with their feelings towards their new child. Simple effective help can resolve this, if it is offered. We want to find out if it is possible to identify which pregnant women are likely to experience problems bonding with their new baby. If these mothers can be identified early, they can be offered effective support when they need it.

We will be asking pregnant women to complete some short questionnaires telling us about how they feel at 36 weeks gestation. We will also ask for some saliva samples to measure the concentration of two natural products. The levels of these two products (cortisol and alpha-amylase) have been shown to change in people who are experiencing emotional disturbance such as anxiety or depression. We will also ask the women taking part to fill in the questionnaires and give another set of saliva samples 6 weeks after the baby is born to compare with their original results. Comparing these will show whether we can predict before the baby is born who is likely to need extra help.

Why have I been chosen?

We are asking all pregnant women at Queen Charlotte's & Chelsea Maternity Hospital who are 36 weeks pregnant to see if they would like to take part. We plan to recruit up to 300 women in total.

What will happen to me if I take part?

We will ask you to take home a saliva sample pack to collect 8 samples of saliva and return them to the research team at your next antenatal appointment. When you next visit the hospital, we will ask you to complete some short questionnaires telling us about how you feel. This will take approximately 20 minutes.

After the baby is born we will contact you by letter or telephone and ask you to complete a similar set of questionnaires and give another set of saliva samples. We will post the questionnaires and sample kits to you so that you can return them with you when you attend your normal postnatal appointment. This will be approximately 6 weeks after the baby is born.

If, during the course of the study, either before or after your baby is born, we identify that you are feeling particularly anxious, stressed or depressed and may benefit from talking to someone who can give you further support we will ask if you would like us to refer you to the appropriate health professional in your area. The counselling service accessible through Queen Charlotte's Hospital is available if you live in Hammersmith or Fulham, otherwise you will be referred to your own GP for services in your area.

What are the possible benefits of taking part?

There is no intended direct clinical benefit from taking part in the study. However, information from the study will help us to understand more about stress and detect early failure to bond. This in turn may help these women to benefit from early intervention methods.

What if something goes wrong?

We do not believe that there are any possible risks or disadvantages in taking part and we do not anticipate anything going wrong.

However, in the very unlikely event of your suffering any adverse effects as a consequence of your participation in this study, you will be compensated through the Imperial College School of Medicine's "No Fault" Compensation Scheme.

Will my taking part in this study be kept confidential?

Results from the study will not contain any personal information. All information collected during the course of the research will be kept strictly confidential. All samples will be anonymous for the laboratory work, and therefore, your name will not be linked to the sample. The only people who will be able to identify you are members of the research team. We will let your GP know that you are taking part in the study but no information you provide us will be passed on to him/her.

What will happen to the results of the research study?

We intend to publish the findings of this research in a medical/scientific journal.

Your choice

You do not have to join the study. It is up to you to decide whether or not to take part. If you do decide to participate you will be given this information sheet to keep and we will ask you to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw, or a decision to take part, will not affect the standard of care you receive. Please ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to join the study and feel free to discuss your decision with others. We will be happy to let you have a copy of the leaflet entitled 'Medical Research and You' published by Consumers for Ethics in Research (CERES). This leaflet gives more information about medical research and looks at some questions you may want to ask.

Who is organising and funding the research?

Professor Vivette Glover, Dr Alyx Taylor-Vieira and Ms Bennie Agbagwara RM, MSc, PhD student are organising the study which is funded by the Institute of Obstetrics and Gynaecology Trust.

The study has been approved by the Hammersmith, Queen Charlotte's & Chelsea Hospitals Research Ethics Committee.

Thank you for taking the time to read this information sheet.

Appendix 9 Study Information Sheet Version 2

Prediction and biological correlates of poor mother-infant bonding in new mothers (Mother-to-infant bonding)

You are invited to take part in a research study

Please take time to read the following information carefully and discuss it with others if you wish. Before you decide whether to take part or not, it is important for you to understand why the research is being done and what it will involve.

What is the purpose of the study?

Pregnancy may cause some women to experience emotional disturbance, for example anxiety or depression. Some mothers find that they have difficulties with their feelings towards their new child. Simple effective help can resolve this, if it is offered. We want to find out if it is possible to identify which pregnant women are likely to experience problems bonding with their new baby. If these mothers can be identified early, they can be offered effective support when they need it.

We will be asking all pregnant women taking part in this study to complete some short questionnaires telling us how they feel from 36 weeks gestation. We will also ask the women taking part to fill in another set of questionnaires 6 weeks after the baby is born to compare with their original results. Comparing these will show whether we can predict before the baby is born who is likely to need extra help.

Why have I been chosen?

We are asking all pregnant women at Queen Charlotte's & Chelsea Maternity Hospital who are 28- 36 weeks pregnant to see if they would like to take part. We plan to recruit up to 400 women in total.

What will happen to me if I take part?

We will ask you to complete some short questionnaires at home when you are 36 weeks pregnant. This will take approximately 20 minutes. You may also wish to complete these questionnaires in the hospital while waiting to be called for your appointment. We will ask you to return the completed questionnaires to the research team at your next antenatal appointment or post it with stamped addressed envelope provided by the research team.

After your baby is born we will contact you by letter or telephone and ask you to complete a similar set of questionnaires. We will post the questionnaires to you. The questionnaires completed at 6 weeks postpartum will be posted back to the hospital in a stamped addressed envelope provided by the research team. This will be

approximately 6 weeks after your baby is born.

If, during the course of the study, either before or after your baby is born, we identify that you are feeling particularly anxious, stressed or depressed and may benefit from talking to someone who can give you further support we will ask if you would like us to refer you to the appropriate health professional in your area. The counselling service is accessible through West London Centre for Counselling, if you live or work in Hammersmith or Fulham, otherwise you will be referred to your own GP for services in your area.

What are the possible benefits of taking part?

There is no intended direct clinical benefit from taking part in the study. However, information from the study will help us to understand more about stress and detect early failure to bond. This in turn may help these women to benefit from early intervention methods.

What if something goes wrong?

We do not believe that there are any possible risks or disadvantages in taking part and we do not anticipate anything going wrong.

However, in the very unlikely event of your suffering any adverse effects as a consequence of your participation in this study, you will be compensated through the Imperial College School of Medicine's "No Fault" Compensation Scheme.

Will my taking part in this study be kept confidential?

Results from the study will not contain any personal information. All information collected during the course of the research will be kept strictly confidential. All questionnaires will be anonymous and therefore, your name will not be linked to the questionnaire. The only people who will be able to identify you are members of the research team. We will let your GP know that you are taking part in the study in case you need extra follow-up but no information you provide us will be passed on to him/her.

What will happen to the results of the research study?

We intend to publish the findings of this research in a medical/scientific journal.

Your choice

You do not have to join the study. It is up to you to decide whether or not to take part. If you do decide to participate you will be given this information sheet to keep and we will ask you to sign a consent form. If you decide to take part you are still free to

withdraw at any time and without giving a reason. A decision to withdraw, or a decision to take part, will not affect the standard of care you receive. Please ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to join the study and feel free to discuss your decision with others. We will be happy to let you have a copy of the leaflet entitled 'Medical Research and You' published by Consumers for Ethics in Research (CERES). This leaflet gives more information about medical research and looks at some questions you may want to ask.

Thank you for taking the time to read this information sheet.

Who is organising and funding the research?

Professor Vivette Glover

Imperial College London

Professor Debra Bick; Dr Alyx Taylor-Vieira and MS Bennie Agbagwara RM, MSc,
PhD Student

Kings College London

The study is funded by the Institute of Obstetrics and Gynaecology Trust.

The study has been approved by the Charing Cross Hospital Research Ethics Committee.

Appendix 10 Notice of substantial amendment 1

NOTICE OF SUBSTANTIAL AMENDMENT

For use in the case of all research other than clinical trials of investigational medicinal products (CTIMPs). For substantial amendments to CTIMPs, please use the EU-approved notice of amendment form (Annex 2 to ENTR/CT1) at <http://eudract.emea.eu.int/document.html#guidance>.

To be completed in typescript by the Chief Investigator in language comprehensible to a lay person and submitted to the Research Ethics Committee that gave a favourable opinion of the research ("the main REC"). In the case of multi-site studies, there is no need to send copies to other RECs unless specifically required by the main REC.

Further guidance is available at

<http://www.nres.npsa.nhs.uk/applicants/review/after/amendments.htm>.

Details of Chief Investigator:	
Name:	Professor Vivette Glover
Address:	Professor of Perinatal Psychobiology Imperial College London Institute of Reproductive and Developmental Biology Du Cane Road London W12 0NN
Telephone:	02075942136
Email:	v.glover@imperial.ac.uk
Fax:	02075942138
Full title of study:	Prediction and biological correlates of poor mother-infant bonding in new mothers.
Name of main REC:	Charing Cross Research Ethics Committee
REC reference number:	07/H0711/97
Date study commenced:	23/01/2008
Protocol reference (<i>if applicable</i>), current version and date:	
Amendment number and date:	

<p>Type of amendment (indicate all that apply in bold)</p> <p>(a) Amendment to information previously given on the NRES Application Form</p> <p>Yes</p> <p>(b) Amendment to the protocol</p> <p>Yes</p> <p>(c) Amendment to the information sheet.</p> <p>Yes</p> <p>Version 2: March 2008.</p>											
<p>Is this a modified version of an amendment previously notified to the REC and given an unfavourable opinion? <i>No</i></p>											
<p>Summary of changes</p> <p>The researcher will visit research participants at home with their one-to-one midwives in order to recruit women who have their antenatal care at home. The researcher will visit participants GP's clinics at 6 weeks post-partum in order to collect post natal samples from the participants. This is the most convenient location for the women who do not come back to Queen Charlotte's Antenatal Clinic.</p>											
<p>Any other relevant information</p> <p>Applicants may indicate any specific ethical issues relating to the amendment, on which the opinion of the REC is sought.</p>											
<p>List of enclosed documents</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 50%;">Document</th> <th style="width: 20%;">Version</th> <th style="width: 30%;">Date</th> </tr> </thead> <tbody> <tr> <td>Participant information sheet</td> <td>2</td> <td>March 2008</td> </tr> <tr> <td>Research protocol</td> <td></td> <td></td> </tr> </tbody> </table>			Document	Version	Date	Participant information sheet	2	March 2008	Research protocol		
Document	Version	Date									
Participant information sheet	2	March 2008									
Research protocol											



National Research Ethics Service
Charing Cross Research Ethics Committee

Room 4W/12, 4th Floor
Charing Cross Hospital
Fulham Palace Road
London W6 8RF
Tel: 020 8846 7283
Fax: 020 8846 7280

Professor Vivette Glover
Professor of Perinatal Psychobiology
Institute of Reproductive and Developmental Biology
Du Cane Road
London, W12 0NN

10 April 2008

Dear Professor Glover

Study title: Prediction and biological correlates of poor mother-infant bonding in new mothers
REC reference: 07/H0711/97
Amendment number: 1
Amendment date: 04 February 2008

The above amendment was reviewed at the meeting of the Sub-Committee of the REC held on 04 April 2008.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Protocol	2	
Participant Information Sheet	2	06 March 2008
Notice of Substantial Amendment (non-CTIMPs)	1	06 March 2008
Covering Letter		06 March 2008

Membership of the Committee

The members of the Committee who were present at the meeting are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

This Research Ethics Committee is an advisory committee to London Strategic Health Authority
The National Research Ethics Service (NRES) represents the NRES Directorate within
the National Patient Safety Agency and Research Ethics Committees in England



National Patient Safety Agency

National Research Ethics Service

NOTICE OF SUBSTANTIAL AMENDMENT

For use in the case of all research other than clinical trials of investigational medicinal products (CTIMPs). For substantial amendments to CTIMPs, please use the EU-approved notice of amendment form (Annex 2 to ENTR/CT1) at <http://eudract.emea.eu.int/document.html#guidance>.

To be completed in typescript by the Chief Investigator in language comprehensible to a lay person and submitted to the Research Ethics Committee that gave a favourable opinion of the research ("the main REC"). In the case of multi-site studies, there is no need to send copies to other RECs unless specifically required by the main REC.

Further guidance is available at <http://www.nres.npsa.nhs.uk/applicants/review/after/amendments.htm>.

Details of Chief Investigator:

Name: Professor Vivette Glover
Address: Professor of Perinatal Psychobiology
 Imperial College London
 Institute of Reproductive and Developmental
 Biology
 Du Cane Road
 London W12 0NN

Telephone: 02075942136
Email: v.glover@imperial.ac.uk
Fax: 02075942138

Full title of study:	Prediction and biological correlates of poor mother-infant bonding in new mothers.
Name of main REC:	Charing Cross Research Ethics Committee
REC reference number:	07/H0711/97
Date study commenced:	23/01/2008
Protocol reference (if applicable), current version and date:	

Type of amendment (indicate all that apply in bold)

(a) Amendment to information previously given on the NRES Application Form

No

(b) Amendment to the protocol

No

If yes, please submit either the revised protocol with a new version number and date, highlighting changes in bold, or a document listing the changes and giving both the previous and revised text.

(c) Amendment to the information sheet(s) and consent form(s) for participants, or to any other supporting documentation for the study

No


If yes, please submit all revised documents with new version numbers and dates, highlighting new text in bold.

Is this a modified version of an amendment previously notified to the REC and given an unfavourable opinion?

No

Summary of changes

The researcher will also recruit from the medical disorders clinic at Queen Charlotte's and Chelsea Hospital

	 National Research Ethics Service Charing Cross Research Ethics Committee Room 4W/12, 4th Floor Charing Cross Hospital Fulham Palace Road London, W6 8RF Telephone: 020 8846 7283 Facsimile: 020 8846 7280						
 Professor Vivette Glover Professor of Perinatal Psychobiology Institute of Reproductive and Developmental Biology Du Cane Road London, W12 0NN							
12 September 2008							
Dear Professor Glover							
Study title:	Prediction and biological correlates of poor mother-infant bonding in new mothers						
REC reference:	07/H0711/97						
Amendment number:	2						
Amendment date:	12 August 2008						
<p>The above amendment was reviewed at the meeting of the Sub-Committee of the REC held on 11 September 2008.</p>							
Ethical opinion							
<p>The members of the Committee present gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.</p>							
Approved documents							
<p>The documents reviewed and approved at the meeting were:</p>							
<table border="1" style="width: 100%;"><thead><tr><th>Document</th><th>Version</th><th>Date</th></tr></thead><tbody><tr><td>Notice of Substantial Amendment (non-CTIMPs)</td><td></td><td>12 August 2008</td></tr></tbody></table>		Document	Version	Date	Notice of Substantial Amendment (non-CTIMPs)		12 August 2008
Document	Version	Date					
Notice of Substantial Amendment (non-CTIMPs)		12 August 2008					
Membership of the Committee							
<p>The members of the Committee who were present at the meeting are listed on the attached sheet.</p>							
R&D approval							
<p>All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.</p>							
Statement of compliance							
<p>The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.</p>							
<small>This Research Ethics Committee is an advisory committee to London Strategic Health Authority The National Research Ethics Service (NRES) represents the NRES Directorate within the National Patient Safety Agency and Research Ethics Committees in England</small>							

Appendix 14 Participant Consent Form

Rec no. 07/H0711/97

Version 1: Dec. 2007

Prediction and biological correlates of poor mother-to-infant bonding in new mothers

In order to confirm your willingness to take part, as is standard in medical research, we would be grateful if you would read, complete, sign and return one copy of this form.

This study has been explained to me by _____

I confirm that I have read and understood the information sheet for the above study, and have had the opportunity to ask questions. I understand what is required from me to take part in this study.

☐ ☐

I am willing to complete the questionnaires for this study.

☐ ☐

I am willing to give saliva samples. I understand that the samples will be used to measure amylase and cortisol levels as described in the information sheet given to me.

☐ ☐

I agree to the study team looking at my medical records or contacting doctors who have treated me (including my GP)

☐ ☐

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving reason, and without my medical care being affected.

Signature _____ Date _____

Name in Capitals _____

Investigator's Signature _____ Date _____

Name in Capitals _____

Imperial College London

Institute of Reproductive and Developmental Biology

Hammersmith Campus

Du Cane Road,
London W12 ONN

Tel: +44 (0) 207 594 2159

Mobile: 07737002462

benedicta.agbagwara05@imperial.ac.uk

16th April 2008

Re: Prediction and biological correlates of poor mother-infant bonding in new mothers.

The above study was introduced to you at your Action group meeting held on 30th January 2008 by Prof. V Glover and myself.

We have now got the Ethics approval to work with the one to one midwives on the above study. Your role has been highlighted in the research protocol.

We are now ready to start recruiting with the one-to-one midwives. Please could you inform the women in your caseload about the study and contact me when you have any woman who wants to do the study. I am usually recruiting at Queen Charlotte's Antenatal clinic on Tuesdays and Wednesdays. I will either visit them at home with you or see them in one of those days that I am recruiting in the clinic.

The saliva sample and questionnaires will be done at 36 weeks gestation, ideally I will like to meet them once between 30 – 35 weeks gestation in order to explain the study to them and get their consent before 36 weeks gestation when the saliva sample and questionnaires will be collected.

Thank you for your help in this study.

Yours faithfully,

Bennie Agbagwara

Research assistant, PhD student

Appendix 16 Study leaflet

Who is organising this research?

The research is being led by a PhD student with the support of researchers from Imperial College and King's College London

Professor Vivette Glover
Imperial College London
Hammersmith Campus

Professor Debra Bick
Dr Alyx Taylor-Vieira
King's College London

The study has been approved by Charing Cross Hospital Research Ethics Committee.
REC reference no. 07/H0711/97





Mother-to-infant bonding study



If you are interested in this study, please contact

Bennie Agbagwara RGN, RM, MSc
PhD Student

Ground floor
IRDB
Imperial College London
Hammersmith Campus
Du Cane Road
London W12 0NN

020 7594 2188
Mobile: 07737 002 462
benedicta.agbagwara05@imperial.ac.uk

We are conducting a study at this hospital, which is looking at whether women who may experience difficulties with their feelings towards their new baby could be identified in pregnancy.


We are inviting all pregnant women at Queen Charlotte's & Chelsea Maternity Hospital who are 20- 38 weeks pregnant to take part in this study.

What is the purpose of the study?

Pregnancy may cause some women to experience emotional problems, for example feelings of anxiety, stress or depression. Some mothers also find that they have difficulties with their feelings towards their new baby. The term 'bonding' is often used to describe these feelings.

If women who experience emotional problems or difficulties with their feelings towards their baby are identified it is possible to offer a range of support and help.


We are conducting a study to find out if it is possible to identify which pregnant women who are likely to experience difficulties with their feelings towards their new baby to enable them to be offered timely and appropriate support when they need it.



What would be involved in taking part?



Women who agree to take part will be asked to complete a short questionnaire telling us how they feel when they are around 35 weeks pregnant. In addition, we will also ask each woman to take a sample of their saliva to return with their questionnaire, which we will use to measure the levels of two natural products (which are called cortisol and alpha-amylase) found in human saliva.

We are asking for saliva samples, as we are interested in finding out if women experiencing emotional problems in pregnancy have changes in levels of these natural products. This is because the levels of these two products (cortisol and alpha-amylase) have been shown to change in people who are experiencing emotional disturbance such as anxiety, stress or depression.



Women taking part in our study will also be asked to fill in another questionnaire and provide another set of their saliva samples at 6 weeks after the baby is born. These findings will be compared with the findings from the questionnaire and saliva samples at 35 weeks of pregnancy.

Comparing these will show whether we can predict before the baby is born women who may need extra help and support to cope with their feelings. The findings of our study will be used to improve care of women in the future.

	
Ms. Bennie Agbagwara	
4th Floor Institute of Reproductive & Developmental Biology	
Hammersmith Campus	
Du Cane Road,	
London, W12 0NN	
v.glover@imperial.ac.uk	
alyx.taylor@imperial.ac.uk	
benedicta.agbagwara05@Imperial.ac.uk	
Dear Dr	
Prediction and biological correlates of poor mother-infant bonding in new mothers	
Re:	D.O.B
<p>The above named patient has been invited to participate in a study to determine whether women who go on to have difficulty bonding with their new infants can be identified before the baby is born. This is being co-ordinated by Institute of Reproductive & Developmental Biology, Hammersmith Hospital, Imperial College and Kings College London. The patient was recruited at Queen Charlotte's & Chelsea Maternity Hospital antenatal clinic at 36 weeks gestation.</p>	
<p>The research involves the completion of self-rating questionnaires and collection of saliva samples. Further details of this project are given in the attached information sheet that has also been given to your patient.</p>	
<p>If you have any concerns or questions about this study, please do not hesitate to contact Professor Vivette Glover, Dr Alyx Taylor or myself.</p>	
Yours sincerely	
Bennie Agbagwara	
Research Assistant /PhD student	

	
Ms. Bennie Agbagwara	
4 th Floor	
Institute of Reproductive & Developmental Biology	
Hammersmith Campus	
Du Cane Road,	
London, W12 0NN	
benedicta.agbagwara05@Imperial.ac.uk	
Tel: 0207 594 2188/ 07737002462	
Dear	
Re: Prediction and biological correlates of poor mother-infant bonding in new mothers (Mother to infant bonding study).	
<p>Thanks for agreeing to take part in the above study. I would be very grateful if you could complete the enclosed questionnaires when you are 36 weeks pregnant. However, if you are more than 36 weeks pregnant please complete these questionnaires as soon as possible before your baby is born. We need both your antenatal and postnatal questionnaires to be able to complete the study.</p>	
<p>Please return the completed questionnaires in the enclosed stamped addressed envelope. Do not hesitate to contact me if you require further information.</p>	
<p>Thank you very much for helping us with this study.</p>	
Yours truly,	
<p>Bennie Agbagwara Research assistant /PhD student</p>	

	
Ms. Bennie Agbagwara	
4 th Floor	
Institute of Reproductive &	
Developmental Biology	
Hammersmith Campus	
Du Cane Road,	
London, W12 0NN	
benedicta.agbagwara05@Imperial.ac.uk	
Tel: 0207 594 2188 / 07944861407	
Dear	
Re: Prediction and biological correlates of poor mother-infant bonding in new mothers (Mother to infant bonding study).	
Congratulations on the birth of your baby. I hope that both of you are doing well. Thank you for completing your antenatal questionnaire for the above study.	
Please complete the enclosed questionnaire when your baby is 6 weeks old or as soon as possible if your baby is already 6 weeks old. We will not be able to use your antenatal questionnaire without the postnatal questionnaire as we need both antenatal and postnatal questionnaires to complete the study.	
Please return the completed questionnaire in the enclosed self-addressed envelope. Thanks again for helping us with this study. We really appreciate your effort in taking part in the above study. Any problem, please contact me on 07944861407 / 02075942188 or by email: benedicta.agbagwara05@imperial.ac.uk or Nicole: nicole.king07@imperial.ac.uk	
Yours faithfully, Bennie Agbagwara Research assistant/PhD student	



**Imperial College
London**

Ms. Bennie Agbagwara

4th Floor Institute of Reproductive &

Developmental Biology

Hammersmith Campus

Du Cane Road,

London, W12 0NN

benedicta.agbagwara05@Imperial.ac.uk

Tel: 0207 594 2188 / 07944861407

Dear

Re: Prediction and biological correlates of poor mother-infant bonding in new mothers (Mother to infant bonding study).



Thank you for helping us with the above study. By returning your questionnaire, we noticed from your responses that you seemed a bit up and down in your emotions. You may benefit from talking to someone about how you are feeling.



If you are still feeling like this, perhaps we can offer some advice. If you just feel like talking to somebody about how you have been feeling, do contact your health visitor or G.P, who are there to help you.

If you feel that you need more than just a chat and helpful advice, we can refer you to your GP, health visitor or West London Centre for Counselling, if you live or work in Hammersmith or Fulham. We just need your permission to refer you to these services that will be able to help.

If you have any concerns or questions, please do not hesitate to contact me on 02075942188.

Yours faithfully,
Bennie Agbagwara
Research assistant/PhD student

	
Ms. Bennie Agbagwara	
4th Floor Institute of Reproductive & Developmental Biology	
Hammersmith Campus	
Du Cane Road,	
London, W12 0NN	
benedicta.agbagwara05@Imperial.ac.uk	
Tel: 0207 594 2188 / 07944861407	
Dear	
Re: Prediction and biological correlates of poor mother-infant bonding in new mothers (Mother to infant bonding study).	
<p>Thank for agreeing to take part in the above study. We recently sent you the antenatal questionnaire pack for this study but unfortunately, we have not received your completed questionnaire. Enclosed is another questionnaire pack in case you no longer have the previous one.</p>	
<p>Please complete the enclosed questionnaire as soon as possible. We need both antenatal and postnatal questionnaires to complete the study. Please return the completed questionnaire in the enclosed self-addressed envelope.</p>	
<p>Thanks again for helping us with this study. We really appreciate your effort in taking part in the above study. Any problem, please contact me on 07944861407 / 02075942188 or by email: benedicta.agbagwara05@imperial.ac.uk. Nicole: nicole.king07@imperial.ac.uk</p>	
Yours faithfully,	
Bennie Agbagwara Research assistant/PhD student	

	
Ms. Bennie Agbagwara	
4th Floor Institute of Reproductive & Developmental Biology	
Hammersmith Campus	
Du Cane Road, London, W12 0NN	
benedicta.agbagwara05@Imperial.ac.uk Tel: 0207 594 2188 / 07944861407	
Dear	
<p>Re: Prediction and biological correlates of poor mother-infant bonding in new mothers (Mother to infant bonding study).</p> <p>Congratulations on the birth of your baby. I hope that both of you are doing well. Thank you for completing your antenatal questionnaire for the above study.</p> <p>We recently sent you the postnatal questionnaire for this study but unfortunately, we have not received your completed questionnaire. Enclosed is another questionnaire pack in case you no longer have the previous one.</p> <p>Please complete the enclosed questionnaire as soon as possible. It does not matter, if your baby is more than 6 weeks old, we can still use your postnatal questionnaire to compare with your completed antenatal questionnaire. We will not be able to use your antenatal questionnaire without the postnatal questionnaire. We need both antenatal and postnatal questionnaires to complete the study.</p> <p>Please return the completed questionnaire in the enclosed self-addressed envelope.</p> <p>Thanks again for helping us with this study. We really appreciate your effort in taking part in the above study. Any problem, please contact me on 07944861407 / 02075942188 or by email: benedicta.agbagwara05@imperial.ac.uk. Nicole: nicole.king07@imperial.ac.uk</p> <p>Yours faithfully,</p> <p>Bennie Agbagwara Research assistant/PhD student</p>	

INSTRUCTIONS FOR THE COLLECTION OF SALIVA SAMPLES.

You will be collecting 4 samples a day, at different times, on 2 consecutive days.

Sample 1 should be taken first thing in the morning, immediately on waking

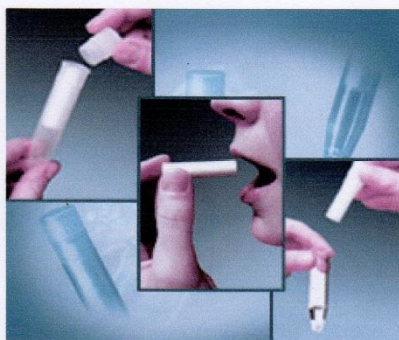
Sample 2 should be taken 30 minutes after waking

Sample 3 should be taken 8 hours after waking

Sample 4 should be taken 12 hours after waking.

Repeat the above on day 2

It is very important that you do not eat, drink or clean your teeth for at least 30 minutes prior to the collection of a saliva sample.



METHOD OF COLLECTION. (See diagram above)

1. First wash your hands.
2. Start by finding the right tube for the right day/time of day, starting with day1, sample 1 at waking on day 1.
3. Remove the lid from the tube and take out the cotton wool roll.
4. Carefully place this under the tongue, behind the bottom front teeth and leave it there for 2 minutes. It will feel rather large and strange to start with, but softens as the saliva is produced. You should sit still during this time.
5. After 2 minutes remove the cotton wool roll from under the tongue, return it to the tube and put the cap back on firmly. It should click once it is properly sealed.
6. **Label clearly with NAME, DATE and TIME OF DAY**
7. Place in an ordinary freezer, or freezer compartment of a fridge
8. Collect each sample in the appropriately labelled tube at the correct time of day as set out in the timetable above.

RETURNING THE SAMPLES.

Once all eight samples have been collected **and frozen**, it is time to return them to post it with the stamped addressed envelop provided.



Saliva Samples Record Sheet

Participant ID:

Date

e.g. 26.03.07

Please take your samples during the week not at weekend

Time you took sample		hours	minutes
Sample 1	wakening	time	<input type="text"/> : <input type="text"/>
Sample 2	30 minutes post waking	time	<input type="text"/> : <input type="text"/>
Sample 3	8 hours post waking	time	<input type="text"/> : <input type="text"/>
Sample 4	12 hours post waking	time	<input type="text"/> : <input type="text"/>

If you forget to do a sample and have to do it on another time, please state which sample this was and when you did it.

Please read the instruction sheet before you start

Use the correct tube for each sample

After you have done each sample make sure the lid is on tight

Write the date and time of sample in **each tube**

Put the tube in the plastic bag provided and then into the fridge

Please keep your samples refrigerated until you return them to us

Don't forget to put this form in with the saliva tubes when you return them

Thank you very much for helping us with
this study

Appendix 25 Ethnic group classification

Ethnicity Groups classification

What is your ethnicity Groups?

Please choose one option that best describes your ethnic group or background:

White:	A White British
	B White Irish
	C Any other White background
Mixed:	D White and Black Caribbean
	E White and Black African
	F White and Asian
	G Any other mixed background
Asian or Asian British:	H Indian
	J Pakistani
	K Bangladeshi
	R Chinese
	L Any other Asian background
Black or Black British:	M Caribbean
	N African
	P Any other Black background
Other Ethnic group:	S Arab
	Z Any other ethnic group not stated.

<http://www.ons.gov.uk/ons/guide-method/measuring-equality/equality/ethnic-national-identity-religion/ethnic-group/index.html>

Appendix 26 Personal details medical and obstetric information on recruitment

**Prediction and biological correlates of mother-infant bonding in new mothers.
REC. No: 07/H0711/97 : Participants details**

TODAY'S DATE

SURNAME

FIRST NAME

HOSP NUMBER

STUDY NO:

DATE OF BIRTH

AGE

ADDRESS

DAYTIME

TELEPHONE

EVENING

TELEPHONE

GP NAME

ADDRESS

Born in this country: Yes / NO

Participants occupation

Partner's occupation

Occupational status : Not currently working / Working part time
/ Full time

Is your job professional/ managerial / skilled / non skilled?

Highest level of education: Non / GCSE/ A Level's / Degree/
Higher degree

Cigarettes/ day

Alcohol: units/
week

Who is living with you, Husband / Partner/ Other relatives/
Alone?

Prescribed drugs or cream

Any medical or obstetric problem in the current pregnancy?

Miscarriage:

Appendix 27 Postnatal data collection form

Prediction and biological correlates of poor mother-infant bonding in new mothers
(Mother-to-infant bonding study)

Registration No: 07/H0711/97

Study No:

Date

Tel No. home:

Mobile:

Living with:

Cigarettes/day:

Alcohol: units/week

Baby details

Baby DOB:

Male / Female

Gestational age at birth:

Birth weight:

Mode of delivering: Normal birth / Elective or Emergency caesarean section / Ventous
/ Forceps

How painful was your delivering on the scale of 1 – 5, 5 being very painful and 0 not
painful: (0) (1) (2) (3) (4) (5).

What type of pain relief did you have during labour?: None / Tens machine/

Gas and air / Epidural / Spinal / GA.

Method of feeding at birth: Breast / Bottle/ mixed feeding

When did you start breastfeeding: Within 0 -1 hour / 1- 4 hours / 5-24 hours / more than
24 hours after birth.

Method of feeding at 6 weeks

How long did you breastfeed your baby?

Date of sample:

How old is your baby now (in weeks)?

Mother's Name:

Study No:

Hospital No:

Baby's d.o.b

Baby's sex:

Baby's weight:

Gestational age:

Head circumference:

Type of delivery:

Length of labour:

Analgesia during labour:

Apgar 1min: 5 mins:

Congenital abnormalities:

Admission to SCBU:

Feeding at discharge:

Other comments:

Appendix 29 Spielberger State Anxiety Inventory

Today's date	Study no.	How many weeks pregnant are you now?
<p>DIRECTIONS: A number of statements which people have used to describe themselves are given below. Read each statement and then tick in the appropriate box on the right to indicate how you feel right now, that is, at this moment. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.</p>		

		Not At All	Somewhat	Moderately	Very much
1	I feel calm				
2	I feel secure				
3	I am tense				
4	I feel strained				
5	I feel at ease				
6	I feel upset				
7	I am presently worrying over possible misfortunes				
8	I feel satisfied				
9	I feel frightened				
10	I feel comfortable				
11	I feel self-confident				
12	I feel nervous				
13	I am jittery				
14	I feel indecisive				
15	I am relaxed				
16	I feel content				
17	I am worried				
18	I feel confused				
19	I feel steady				
20	I feel pleasant				

Spielberger Trait Anxiety Inventory

DIRECTIONS: A number of statements which people have used to describe themselves are given below. Read each statement and then tick in the appropriate box on the right to indicate how you generally feel. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe how you generally feel, even before pregnancy

		Almost never	Sometimes	Often	Almost always
21.	I feel pleasant				
22.	I feel nervous and restless				
23.	I feel satisfied with myself				
24.	I wish I could be as happy as others seem to be				
25.	I feel like a failure				
26.	I feel rested				
27.	I am "calm, cool and collected"				
28.	I feel that difficulties are piling up so that I cannot overcome them				
29.	I worry too much over something that really doesn't matter				
30.	I am happy				
31.	I have disturbing thoughts				
32.	I lack self-confidence				
33.	I feel secure				
34.	I make decisions easily				
35.	I feel inadequate				
36.	I am content				
37.	Some unimportant thought runs through my mind and bothers me				
38.	I take disappointments so keenly that I can't put them out of my mind				
39.	I am a steady person				
40.	I get in a state of tension or turmoil as I think over my recent concerns and interests				

(Spielberger, 1983)

Appendix 30 Edinburgh Postnatal Depression Scale (EPDS)

In the following questions, please tick the answer which comes closest to how you have felt in the past week, not just today.

1	I have been able to laugh and see the funny side of things: As much as I always could Not quite so much now Definitely not so much now Not at all
2	I have looked forward with enjoyment to things: As much as I ever did Rather less than I used to Definitely less than I used to Hardly at all
3	I have blamed myself unnecessarily when things went wrong: Yes, most of the time Yes, some of the time Not very often No, never
4	I have been anxious or worried for no good reason: No, not at all Hardly ever Yes, sometimes Yes, very often
5	I have felt scared or panicky for no very good reason: Yes, quite a lot Yes, sometimes No, not much No, not at all
6	Things have been getting on top of me: Yes, most of the time I haven't been able to cope at all Yes, sometimes I haven't been coping as well as usual No, most of the time I have coped quite well No, I have been Coping as well as ever
7	I have been so unhappy that I have had difficulty sleeping: Yes, most of the time Yes, sometimes Not very often No, not at all
8	I have felt sad or miserable: Yes, most of the time Yes, quite often Not very often No, not at all
9	I have been so unhappy that I have been crying: Yes, most of the time Yes, quite often Only occasionally No, never
10	The thought of harming myself has occurred to me: Yes, quite often Sometimes Hardly ever Never

(Cox et al., 1987)

Appendix 31 Stressful Life Events Scale (SLES)

Listed below are a number of events that may have brought changes in your life. Have any of these events occurred to you since you became pregnant with this baby? If so, please assess how much effect it had on you, and circle whether it was during pregnancy or after you gave birth. If one of these events occurred more than once, please rate the effect on you of the most serious. Many of the events listed are of a personal nature. Your answers will be held in strict confidence.

		No, this has never happened	Yes this has happened, and it affected me a little	Yes this has happened, and it affected me a lot
1	You were admitted to the hospital			
2	You had a serious accident or illness			
3	Your partner had a serious accident or illness			
4	A friend or family member had a serious accident or illness			
5	You were in trouble with the law			
6	Your partner was in trouble with the law			
7	You were separated / divorced			
8	Your partner lost his job			
9	You experienced a significant drop in income			
10	You had a major financial problem			
11	Your car or house was burgled			
12	You became homeless			
13	You found that your partner did not want your child			
14	You had a serious argument with your partner			
15	You had a serious argument with your family or friends			
16	Your partner was physically cruel to you			
17	Your partner was emotionally cruel to you			

18	You were physically cruel to your partner			
19	You attempted suicide			
20	A friend or relative attempted suicide			
21	You suffered from mental illness			
22	A friend or relative suffered from mental illness			
23	Your partner died			
24	A friend or relative died			
25	You had an extramarital sexual affair			
26	Your partner had an extramarital sexual affair			

(Bergman et al., 2007)

Appendix 32 Maternal Antenatal Attachment Scale (MAAS)

These questions are about your thoughts and feelings about the developing baby. Please tick one box only in answer to each question.

1	Over the <u>past</u> two weeks I have thought about, or been preoccupied with the baby inside me:	Almost all the time	Very frequently	Frequently	Occasionally	Not at all
2	Over the <u>past</u> two weeks when I have spoken about, or thought about the baby inside me I got emotional feelings which were:	Very weak or non-existent	Fairly weak	In between strong and weak	Fairly strong	Very strong
3	Over the past two weeks my feelings about the baby inside me have been:	Very positive	Mainly positive	Mixed positive and negative	Mainly negative	Very negative
4	Over the <u>past</u> two weeks I have had the desire to read about or get information about the developing baby. This desire is:	Very weak or non-existent	Fairly weak	Neither strong nor weak	Moderately strong	Very strong
5	Over the past two weeks I have been trying to picture in my mind what the developing baby actually looks like in my womb:	Almost all the time	Very frequently	Frequently	Occasionally	Not at all
6	Over the past two weeks I think of the developing baby mostly as:	A real little person with special characteristics	A baby like any other baby	A human being	A living thing	A thing not yet really alive
7	Over the past two weeks I have felt that the baby inside me is dependent on me for its well-being:	Totally	A great deal	Moderately	Slightly	Not at all
8	Over the past two weeks I have found myself talking to my baby when I am alone	Not at all	Occasionally	Frequently	Very frequently	Almost all the time I am alone
9	Over the past two weeks when I think about (or talk to) my baby inside me, my thoughts:	Are always tender and loving	Are mostly tender and loving	Are a mixture of both tenderness and irritation	Contain a fair bit of irritation	Contain a lot of irritation
10	The picture in my mind of what the baby at this stage actually looks like inside					

These questions are about your thoughts and feelings about the developing baby. Please tick one box only in answer to each question.

	the womb is:	Very clear	Fairly clear	Fairly vague	Very vague	I have no idea at all
11	Over the past two weeks when I think about the baby inside me I get feelings which are:	Very sad	Moderately sad	A mixture of happiness and sadness	Moderately happy	Very happy
12	Some pregnant women sometimes get so irritated by the baby inside them that they feel like they want to hurt it or punish it:	I couldn't imagine I would ever feel like this	I could imagine I might sometimes feel like this, but I never actually have	I have felt like this once or twice myself	I have occasionally felt like this myself	I have often felt like this myself
13	Over the past two weeks I have felt:	Very emotionally distant from my baby	Moderately emotionally distant from my baby	Not particularly emotionally close to my baby	Moderately close emotionally to my baby	Very close emotionally to my baby
14	Over the past two weeks I have taken care with what I eat to make sure the baby gets a good diet:	Not at all	Once or twice when I ate	Occasionally when I ate	Quite often when I ate	Every time I ate
15	When I first see my baby after the birth I expect I will feel:	Intense affection	Mostly affection	Dislike about one or two aspects of the baby	Dislike about quite a few aspects of the baby	Mostly dislike
16	When my baby is born I would like to hold the baby:	Immediately	After it has been wrapped in a blanket	After it has been washed	After a few hours for things to settle down	The next day

These questions are about your thoughts and feelings about the developing baby. Please tick one box only in answer to each question.					
17	Over the past two weeks I have had dreams about the pregnancy or baby:				
	Not at all	Occasionally	Frequently	Very frequently	Almost every night
18	Over the past two weeks I have found myself feeling, or rubbing with my hand, the outside of my stomach where the baby is:				
	A lot of times each day	At least once per day	Occasionally	Once only	Not at all
19	If the pregnancy was lost at this time (due to miscarriage or other accidental event) without any pain or injury to myself, I expect I would feel:				
	Very pleased	Moderately pleased	Neutral (i.e. neither sad nor pleased; or mixed feelings)	Moderately sad	Very sad

(Condon, 1993)

Appendix 33 Standardised Assessment of Personality Abbreviated Scale (SAPAS)

<p>We're interested in learning about your personality, so I'd like to ask you a few questions about yourself. If the way you have been in recent weeks or months is different from the way you usually are, please look back to when you were your usual self.</p>		
	Yes	No
1. <i>In general</i> , do you have difficulty making and keeping friends?		
2. Would you <i>normally</i> describe yourself as a loner?		
3. <i>In general</i> , do you trust other people?		
4. Do you <i>normally</i> lose your temper easily?		
5. Are you <i>normally</i> an impulsive sort of person? (If need clarification: Do you rush into most things without thinking about the consequences?)		
6. Are you <i>normally</i> a worrier?		
7. <i>In general</i> , do you depend on others a lot?		
8. <i>In general</i> , are you a perfectionist? (If need clarification: Does it upset you when things aren't perfect?) (Check that this applies to most tasks – not just isolated areas of their life)		
9. Do you in general have difficulty getting along with people?		

Appendix 34 Mother-to-infant bonding Scale (MIBS)

These questions are about your feelings for your child in the first few weeks. Some adjectives are listed below which describe some of the feelings mothers have towards their baby in the FIRST WEEKS after they were born. Please make a tick against each word in the box which best describes how you felt in the FIRST WEEK.

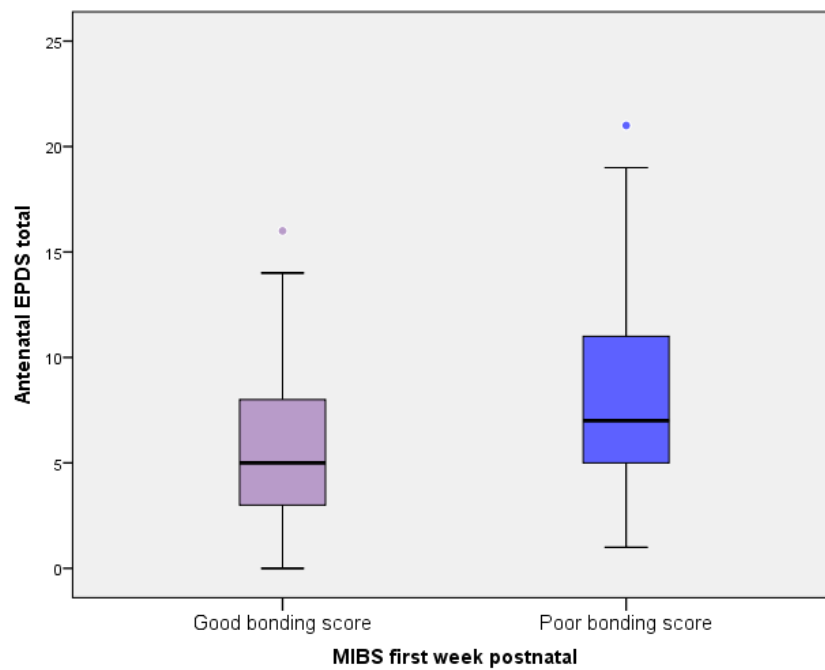
		Very much	A lot	A little	Not at all
1	Loving				
2	Resentful				
3	Neutral or felt nothing				
4	Joyful				
5	Dislike				
6	Protective				
7	Disappointed				
8	Aggressive				

Please make a tick again in the box below against each word in the box which best describes your feelings towards your baby now (6 weeks postnatal)

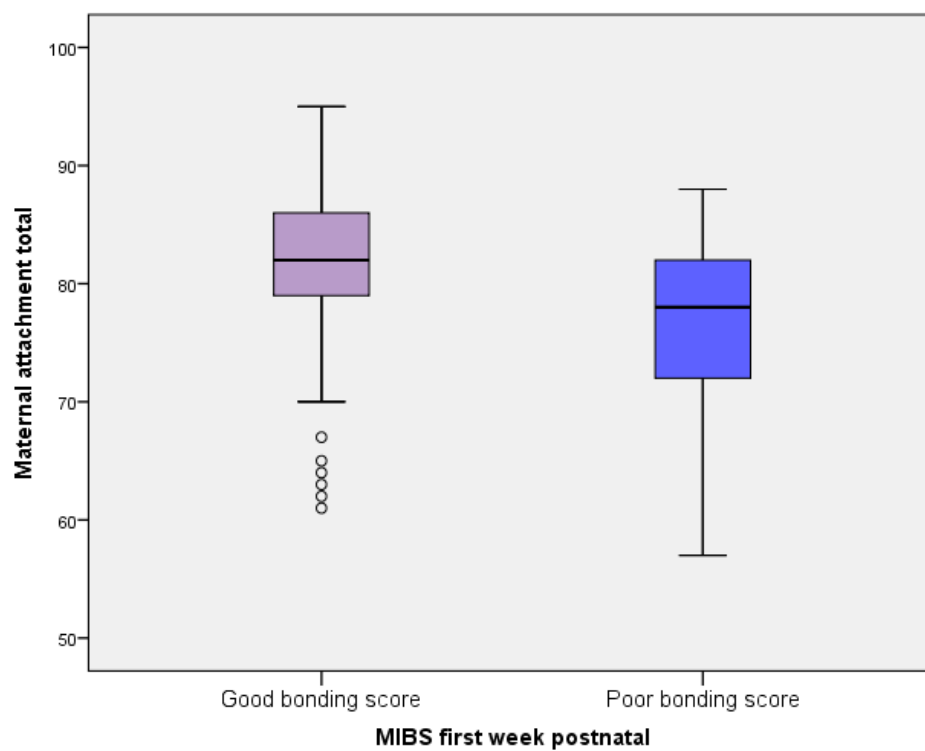
		Very much	A lot	A little	Not at all
1	Loving				
2	Resentful				
3	Neutral or felt nothing				
4	Joyful				
5	Dislike				
6	Protective				
7	Disappointed				
8	Aggressive				

(Taylor et al., 2005)

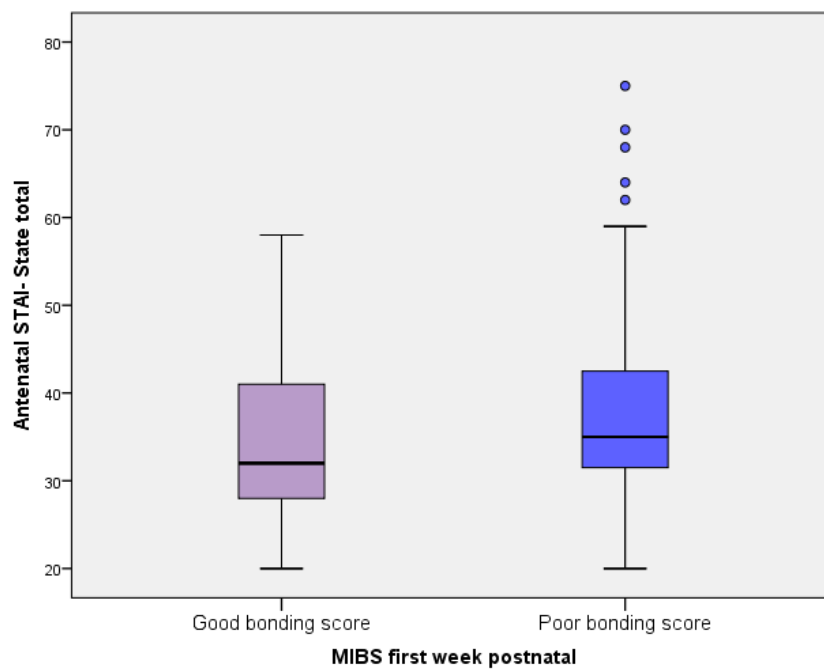
Appendix 35 Boxplots of MAAS (good versus poor bonding score), first week postnatal



Appendix 36 Boxplots of antenatal EPDS total scores (good versus poor bonding) score first weeks postnatal.



Appendix 37 Boxplots of antenatal STAI-State (good versus poor bonding) first week postnatal.



Appendix 38 Boxplots of antenatal STAI-Trait, (good versus poor bonding) first week postnatal

